THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 40 OCTOBER, 1938 No. 4

SEVENTEEN YEARS' EXPERIENCE IN RADIATION THERAPY OF CANCER, ZURICH, 1919–1935*†

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IT IS a great honor for me to open this meeting and to take over its honorary chairmanship.

The most important and at the same time the least satisfactory field for the radiotherapist is the treatment of cancer. Out of this inexhaustible subject I have not chosen one special question; instead the title of my paper will be "*Seventeen Years' Experience in Radiation Therapy of Cancer, Zurich, 1919–1935.*"

Together with my friend and colleague, Zuppinger, I have reviewed all of the material which we have observed during this time. Not one case has been omitted. The number of patients treated is identical with the number of patients observed. This therefore represents a complete survey of all cases sent to us.

It must be appreciated that the Zurich Roentgen Institute is not a place for cancer research but for cancer treatment where we have to admit the incurable patients, whereas the early cases are often treated elsewhere and do not come to our attention. Our report, therefore, represents a true picture of the situation as it actually exists. There has been no selection and the sites of the cancers in different organs, as they are noted in our institute, represent the true occurrence in the population at large.

In Switzerland, the medical mortality statistics are excellently worked out. The cancer incidence is high. With about 4,200,000 inhabitants, 5,696 die during a year from cancer. In the city of Zurich, out of 245,600 inhabitants, 385 die from malignant tumors. In other words, in Switzerland 17 persons die daily from cancer and in the city of Zurich at least one person dies in every twenty-four hours from this disease; that is to say, in Switzerland every eighth and in the city of Zurich every seventh death is a cancer death (see Charts I and II).

Cancer has increased during recent decades whereas infant mortality has decreased enormously, and deaths from tuberculosis are also becoming fewer. In Zurich, cancer represents the most frequent cause of death. This increase of the cancer mortality, however, is not a real increase but is explained as a consequence of the increase in age of the population. The individual today is more endangered from carcinoma, in comparison to his ancestors, only because he now reaches a higher age than they did.

There are great fluctuations in regard to the different sites of cancer in the body. The proportion of cancer of the uterus and stomach has decreased considerably; the proportion of colon, rectum and breast can-

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

† Tables translated from the German by Dr. E. A. Pohle, University of Wisconsin, Madison, Wisconsin.

cer has increased. These fluctuations for different locations cannot be explained at the present time; they seem to have no relation to our therapeutic measures.

The male sex is mainly endangered by carcinoma of the stomach, esophagus, rectum, colon, pharynx and lungs. The overwhelming majority of squamous cell carcinoma occurs in men. The female sex is endangered by carcinoma of the stomach, breast, uterus, ovary, colon and gallbladder. Squamous cell carcinomas are much less frequent than in men, with the exception of cervical carcinoma.

Deaths from sarcoma remain statistically in the background in comparison with deaths from carcinoma, but the mortality from sarcoma also increases steadily with the age.

If we report only those cancers which we can treat successfully with our present methods, operation and irradiation, we obtain an incorrect picture of the situation. I follow in the footsteps of your great pathologist, Ewing, when I report all cases of cancer without selection. It will be interesting for the American scientists to compare the Zurich results with their own, in order to determine whether or not the figures which Ewing offers for the possibility of cancer cure today apply also to our material.

In seventeen years we have treated 2,529 patients with irradiation; 2,464 of these were definite malignant disease; 65 were tumors or borderline malignancies, such as tumors of the hypophysis, of the nervous system, giant cell tumors and pre-

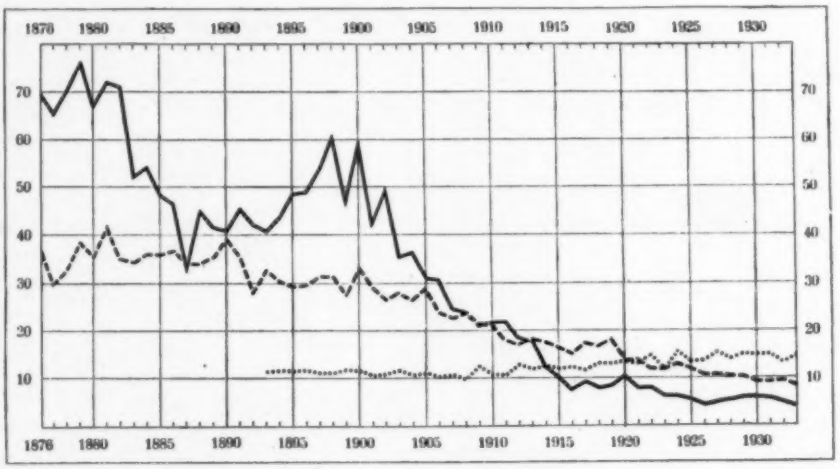

Chart 1. Mortality of babies, from tuberculosis and from cancer 1876–1933. Of 10,000 persons of the average population died: ——— under one year old; - - - - - from tuberculosis; ..... from carcinoma.

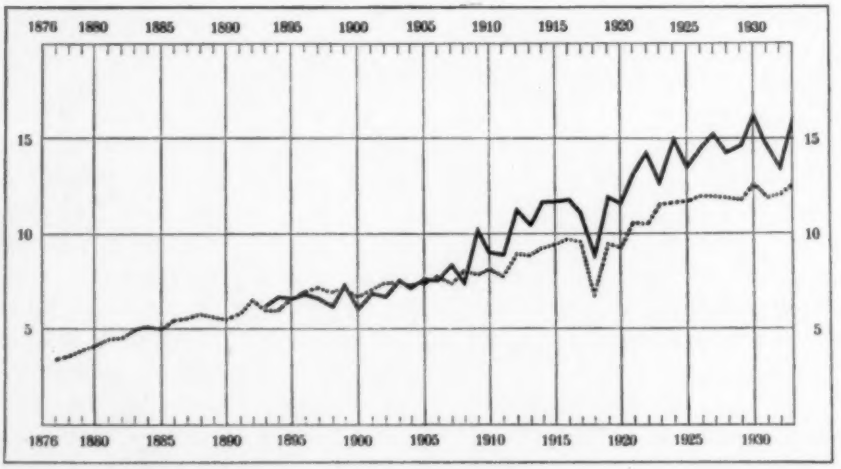

Chart 11. Deaths from carcinoma in per cent of 100 reported deaths ..... Switzerland ——— Zurich.

TABLE I

PATIENTS LIVING ON JANUARY 1, 1937, FREE FROM SYMPTOMS, INCLUDING THOSE DEAD FROM INTERCURRENT DISEASE AFTER THREE YEARS OF OBSERVATION BUT STILL FREE FROM RECURRENCE. OBSERVATION PERIOD: 1919–1935

1 Location of tumor	2 Number of cases	3 Free from symptoms on 1–1–1937	4 Free from symptoms but dead from intercurrent disease after 3 years	5 Total of columns 3 and 4
1. Skin	75	31	3	34
2. Lips	24	10	3	13
3. Orbital region	54	17	12	29
4. Auricular region	9	5	—	5
5. Inner nose and sinuses except maxillary sinuses	21	3	—	3
6. Upper jaw	38	3	1	4
7. Oral cavity	115	27	2	29
8. Parotid	14	5	1	6
9. Epipharynx	41	9	—	9
10. Mesopharynx	252	43	3	46
11. Hypopharynx	239	28	3	31
12. Intrinsic larynx	36	9	—	9
13. Branchiogenic tumors	11	1	—	1
14. Struma maligna	112	14	2	16
15. Breast	403	80	7	87
16. Esophagus	248	3	—	3
17. Stomach	110	5	2	7
18a. Colon	27	3	1	4
18b. Rectum	61	2	2	4
18c. Anus	5	1	—	1
19. Remaining parts of abdomen	28	2	1	3
20. Bronchi and lungs	69	1	—	1
21. Pleura	2	—	—	—
22. Mediastinum	33	4	—	4
23. Kidneys	18	—	—	—
24. Bladder	15	1	—	1
25. Male genitalia	60	11	—	11
26. Female genitalia	61	17	2	19
27. Hypophysis	26	11	—	11
28. Nervous system	27	6	—	6
29. Skeleton	36	5	—	5
30. Other supporting tissue	26	12	1	13
31. Lymph nodes	29	3	—	3
32. Metastases only	188	6	2	8
33. Miscellaneous	4	1	—	1
34. Precancerous lesions	6	2	1	3
35. Giant cell tumors	6	6	—	6
Total	2,529	387 =15.3±0.7%	49 =1.9±0.3%	436 =17.2±0.8%
Total number minus giant cell tumors, precancerous lesions, lesions of nervous system and hypophysis	2,464	362 =14.7±0.7%	48 =1.9±0.3%	410 =16.6±0.8%

cancerous lesions. There were 1,546, or 61 per cent, men and 983, or 39 per cent, women, The average age was 53.6 years (Table 1).

The last day on which the results were checked was January 1, 1937. At that time there were 387 = 15.3 ± 0.7 per cent

alive and symptom-free. After a three-year period had elapsed, $49 = 1.9 \pm 0.3$ per cent were free from symptoms but dead of intercurrent disease. *This represents altogether $436 = 17.2 \pm 0.8$ per cent symptom-free patients.*

TABLE II

CLASSIFICATION OF THE MATERIAL ACCORDING TO LOCALISATION ARRANGED AS TO FREQUENCY (2,529 CASES)

Localisation	Number of cases	Per cent
Upper respiratory and digestive tracts	767	30
Breast	403	16
Esophagus	248	10
Gastrointestinal canal, abdominal organs except ovaries	244	10
Metastases only	188	7
Skin and body orifices	125	5
Struma maligna	112	4
Lungs, bronchi, mediastinum	104	4
Miscellaneous	103	4
Ovaries, testicles, bladder, prostate	90	4
Skeleton	68	3
Nervous system and hypophysis	53	2
Uterus	30	1
Total	2,529	100

All patients who died of intercurrent disease within the three-year period were considered as deaths from cancer. All untraced patients are calculated as cancer deaths. Out of our 2,529 patients 43 or 1.7 ± 0.26 per cent were not traced. Table II shows the main sites of the primary tumors.

We see that in the material of the Zurich Roentgen Institute the cancers of the upper respiratory and digestive tracts are the most frequent types, namely 30 per cent of all cases. They are followed by mammary cancers with 16 per cent, esophageal cancers with 10 per cent, and malignant disease of the intestinal tract and the abdominal organs with 10 per cent each. Cancer of the skin and of the natural openings of the body represent only 5 per cent because the skin cancers are almost exclusively treated in the Dermatologic Clinic in Zurich. There is only 1 per cent cancers of the uterus because these are mainly treated in the Gynecologic Clinic. The small percentage of these cancers of the skin and of the uterus, which are therapeutically favorable cases, naturally lowers our results considerably.

Table III shows the distribution of our material according to the systems of the body. Forty-four per cent of all our patients suffered from cancer of the intestinal tract; only 3 per cent were cancer of the skin and only 6 per cent cancer of the genito-urinary system.

Table IV shows our material in regard to the distribution of the different stages of the disease. We see that out of our 2,529 patients, 600, or 24 per cent, were in an operable stage and 76 per cent in an inoperable condition.

In the operable patients we had a cure rate of 43 per cent; in the inoperable ones of 9 per cent.

TABLE III

CLASSIFICATION OF THE MATERIAL ACCORDING TO ORGAN SYSTEM ARRANGED AS TO FREQUENCY (2,529 CASES)

Localisation	Number of cases	Per cent
Gastrointestinal tract	1,123	44
Breast	403	16
Respiratory tract	251	10
Metastases only	188	7
Urogenital tract	154	6
Struma maligna	112	4
Miscellaneous	96	4
Skin	81	3
Skeleton	68	3
Nervous system and hypophysis	53	2
Total	2,529	100

Only during recent years has histologic examination been developed far enough to allow us to differentiate the more recently classified tumor types. In 1,468 malignant tumors we found 21 basal cell carcinomas, 1,215 other types of carcinoma, 238 sarcomas, 7 mixed tumors, 2 cylindromas and 3 times a carcinoma-sarcomatosis.

Table V shows that we had 38 transitional cell carcinomas. They were located

TABLE IV

CLASSIFICATION OF THE MATERIAL ACCORDING TO THE STAGE OF THE DISEASE

Localisation	Number of cases	Tumors operable	Free from symptoms or dead from intercurrent disease after 3 years	Inoperable tumors	Free from symptoms or dead from intercurrent disease after 3 years
1. Skin	75	46	28+ 3	29	3
2. Lips	24	18	10+ 3	6	—
3. Orbital region	54	43	17+11	11	—+ 1
4. Auricular region	9	4	2	5	3
5. Inner nose	21	2	1	19	2
6. Upper jaw	38	11	1	27	2+ 1
7. Oral cavity	115	41	17+ 1	74	10+ 1
8. Parotid	14	3	2+ 1	11	3
9. Epipharynx	41	3	—	38	9
10. Mesopharynx	252	40	12+ 2	212	31+ 1
11. Hypopharynx	239	16	5	223	23+ 3
12. Intrinsic larynx	36	23	6	13	3
13. Branchiogenic tumors	11	2	1	9	—
14. Struma maligna	112	12	8+ 1	100	6+ 1
15. Breast	403	215	68+ 7	188	12
16. Esophagus	248	—	—	248	3
17. Stomach	110	23	4+ 2	87	1
18. Colon, rectum, anus	93	13	6+ 2	80	—+ 1
19. Remaining parts of abdomen	28	3	1	25	1+ 1
20. Bronchi and lungs	69	—	—	69	1
21. Pleura	2	—	—	2	—
22. Mediastinum	33	—	—	33	4
23. Kidneys	18	3	—	15	—
24. Bladder	15	2	1	13	—
25. Male genitalia	60	13	5	47	6
26. Female genitalia	61	13	7+ 1	48	10+ 1
27. Hypophysis	26	—	—	26	11
28. Nervous system	27	2	1	25	5
29. Skeleton	36	15	4	21	1
30. Other supporting tissue	26	16	9+ 1	10	3
31. Lymph nodes	29	1	—	28	3
32. Metastases only	188	7	2	181	4+ 2
33. Miscellaneous	4	—	—	4	1
34. Precancerous lesions	6	6	2+ 1	—	—
35. Giant cell tumors	6	4	4	2	2
Total	2,529	600	224+36 / 260	1,929	163+13 / 176
Per cent		23.7 ±0.8	43.3 ±2.0	76.3 ±0.8	9.1 ±0.7

in the internal nose, parotid, epipharynx, mesopharynx, hypopharynx and esophagus. We found 23 lympho-epithelial carcinomas. They occurred in the epipharynx, mesopharynx and hypopharynx. Ewing's sarcoma was found 9 times; namely, in the internal nose, in the maxilla, in the oral cavity and in the extremities.

For the radiotherapeutic treatment we have at our disposal in my institute:

1. Interstitial irradiation.
2. Intracavitary radium application.
3. Treatment with the radium mold.
4. The single massive roentgen dose.
5. Scattered fractional postoperative irradiation with roentgen rays.

6. Simple fractional "short time" roentgen therapy.*

7. Simple fractional "long time" roentgen therapy.

The most important method in Zurich is the protracted fractional "long time" irradition. All other procedures are in the background in comparison to this method

TABLE V

ANALYSIS OF HISTOLOGICAL DIAGNOSES IN 1,486 MALIGNANT NEOPLASMS

Localisation	Basal cell carcinoma	Carcinoma				Sarcoma			Mixed tumors	Carcinoma sarcomatodes	Cylindroma
		Squamous cell carcinoma	Transitional cell carcinoma	Lympho-epithelial carcinoma	Carcinoma simplex and adenomatosum	Sarcoma	Melanoma	Ewing's tumor			
Skin	13	33	—	—	1	2	18	—	—	—	—
Lips	2	20	—	—	—	—	—	—	—	—	—
Orbital region	6	14	—	—	10	9	2	—	—	—	—
Auricular region	—	3	—	—	2	3	—	—	—	1	—
Inner nose	—	9	1	—	1	5	1	2	—	—	—
Upper jaw	—	15	—	—	7	4	—	2	—	—	—
Oral cavity	—	88	—	—	5	2	1	1	—	—	1
Parotid	—	—	1	—	3	3	—	—	3	—	1
Epipharynx	—	—	16	16	6	12	—	—	—	—	—
Mesopharynx	—	186	5	5	15	22	1	—	—	—	—
Hypopharynx	—	167	8	2	32	2	—	—	—	—	—
Intrinsic larynx	—	34	—	—	1	—	—	—	—	—	—
Branchiogenic tumors	—	2	—	—	6	—	—	—	—	—	—
Struma maligna	—	1	—	—	37	29	—	—	—	—	—
Breast	—	2	—	—	150	4	—	—	—	—	—
Esophagus	—	127	7	—	22	1	—	—	—	2	—
Stomach	—	—	—	—	34	1	—	—	—	—	—
Colon, rectum	—	—	—	—	22	—	—	—	—	—	—
Anus	—	3	—	—	—	—	—	—	—	—	—
Other abdominal tumors	—	—	—	—	6	13	—	—	—	—	—
Bronchi and lungs	—	7	—	—	10	—	—	—	—	—	—
Pleura	—	—	—	—	2	—	—	—	—	—	—
Mediastinum	—	—	—	—	—	10	—	—	—	—	—
Kidneys	—	—	—	—	5	8	—	—	—	—	—
Bladder	—	—	—	—	6	1	—	—	—	—	—
Male genitalia	—	6	—	—	23	1	—	—	4	—	—
Female genitalia	—	11	—	—	20	4	—	—	—	—	—
Other supporting tissue	—	—	—	—	—	23	—	—	—	—	—
Lymph nodes	—	—	—	—	—	29	—	—	—	—	—
Skeleton	—	—	—	—	—	18	—	4	—	—	—
	21	728	38	23	426	206	23	9	7	3	2

8. Protracted fractional "long time" roentgen therapy.

9. Grenz rays.

* The "short time" refers to a relatively short time treatment period, the term "long time" to a more prolonged poriod, and the term under heading 8 to the original Coutard method.

in point of frequency of employment.

We acknowledge a limited indication for the single massive dose of roentgen rays in small skin cancers, for the intracavitary radium treatment in the uterus and in the oral cavity, for interstitial irradiation and

TABLE VI

GENERAL SURVEY OF PERMANENT RESULTS 1919–1935

Location of tumor	Number of cases	Male	Female	Average age in years	Permanent results of symptom-free cases in per cent		
					1 year	3 years	5 years
1. Skin	75	32	43	57.1	51	39	38
2. Lips	24	22	2	59.2	62	42	50
3. Orbital region	54	33	21	55.5	63	54	49
4. Auricular region	9	4	5	57.8	56	33	33
5. Inner nose and sinuses except maxillary sinuses	21	11	10	51.4	19	13	0
6. Upper jaw	38	20	18	53.9	18	12	16
7. Oral cavity	115	95	20	56.7	31	22	13
8. Parotid	14	10	4	54.2	57	45	22
9. Epipharynx	41	30	11	43.1	27	13	0
10. Mesopharynx	252	233	19	58.4	27	17	11
11. Hypopharynx	239	225	14	58.8	21	10	4
12. Intrinsic larynx	36	35	1	59.4	36	22	24
13. Branchiogenic tumors	11	10	1	58.3	18	0	0
14. Struma maligna	112	59	53	58.1	12	12	12
15. Breast	403	2	401	54.0	41	22	15
16. Esophagus	248	242	6	58.8	2	2	0
17. Stomach	110	59	51	53.3	11	6	5
18a. Colon	27	18	9	48.4	18	13	13
18b. Rectum	61	43	18	58.6	8	10	3
18c. Anus	5	1	4	58.2	20	0	0
19. Remaining parts of abdomen	28	16	12	43.6	18	15	8
20. Bronchi and lungs	69	60	9	58.3	1	0	0
21. Pleura	2	2	—	19.5	0	0	0
22. Mediastinum	33	21	12	38.8	15	11	13
23. Kidneys	18	10	8	31.0	6	0	0
24. Bladder	15	13	2	57.1	20	17	10
25. Male genitalia	60	60	—	51.1	30	16	14
26. Female genitalia	61	—	61	53.0	34	32	26
27. Hypophysis	26	16	10	35.8	46	43	40
28. Nervous system	27	20	7	26.1	22	23	16
29. Skeleton	36	20	16	35.6	19	14	15
30. Other supporting tissue	26	11	15	45.2	69	74	60
31. Lymph nodes	29	17	12	41.6	14	0	0
32. Metastases only	188	86	102	53.3	7	4	3
33. Miscellaneous	4	3	1	40.3	25	25	50
34. Precancerous lesions	6	4	2	55.1	83	75	100
35. Giant cell tumors	6	3	3	37.1	100	100	100
Total	2,529	1,546	983	53.6	24.8 ±0.9	16.6 ±0.8	12.9 ±0.9
Total number minus giant cell tumors, precancerous lesions, lesions of nervous system and hypophysis	2,464	1,503	961	54.1	24.2 ±0.9	15.9 ±0.8	12.1 ±0.9

for the radium mold treatment. For the exclusively palliative treatments the main procedure is a simple fractional "short time" irradiation. In prophylactic postoperative irradiation the scattered fractional "short time" roentgen irradiation appears in the foreground.

Out of our total of 2,529 cases, 506, or 20 per cent, were treated by a combination of radiation and surgery, and 2,023, or

Table VII

GENERAL SURVEY OF THE ONE-YEAR END-RESULTS 1919–1935 IN ABSOLUTE FIGURES

Location of tumor	Number of cases	Permanent cure
1. Skin	75	38
2. Lips	24	15
3. Orbital region	54	34
4. Auricular region	9	5
5. Inner nose and sinuses	21	4
6. Upper jaw	38	7
7. Oral cavity	115	36
8. Parotid	14	8
9. Epipharynx	41	11
10. Mesopharynx	252	68
11. Hypopharynx	239	51
12. Intrinsic larynx	36	13
13. Branchiogenic tumors	11	2
14. Struma maligna	112	14
15. Breast	403	167
16. Esophagus	248	4
17. Stomach	110	12
18a. Colon	27	5
18b. Rectum	61	5
18c. Anus	5	1
19. Remaining parts of abdomen	28	5
20. Bronchi and lungs	69	1
21. Pleura	2	—
22. Mediastinum	33	5
23. Kidneys	18	1
24. Bladder	15	3
25. Male genitalia	60	18
26. Female genitalia	61	21
27. Hypophysis	26	12
28. Nervous system	27	6
29. Skeleton	36	7
30. Other supporting tissue	26	18
31. Lymph nodes	29	4
32. Metastases only	188	14
33. Miscellaneous	4	1
34. Precancerous lesions	6	5
35. Giant cell tumors	6	6
Total	2,529	627 = 24.8 ±0.9%
Total number minus giant cell tumors, precancerous lesions, lesions of nervous system and hypophysis	2,464	598 = 24.2 ±0.9%

80 per cent, by irradiation only. Only 1 per cent of the cases treated by irradiation plus surgery was treated in addition by a radiosurgical procedure, *i.e.*, the simultaneous application of surgery and radiotherapy at the same site of the body. The combination of surgery and irradiation at the same time or successively at different places was applied in 2 per cent of the cases. An example of this type is radiotherapy of the tongue with surgical dissection of the neck. The true combined treatment, meaning operation and postoperative irradiation or preoperative irradiation followed by operation was applied in 96 per cent of the 506 cases.

Out of the 2,023 cases treated with irradiation only in 48 per cent an attempt at a cure was made, and in 50 per cent only palliative procedures were applied. From the point of view of frequency, roentgen therapy is by far the most important procedure in cases treated by irradiation alone. It was indicated in 85 per cent of the cases, radium in only 15 per cent.

What is the reason for this? We have in Zurich no facilities for telecurietherapy and no equipment for high voltage therapy or contact irradiation. The roentgen therapy in our institute is performed with 200 kv. machines.

What are our results? Table VI gives a general survey of the end-results. In our 2,529 tumor cases we have accomplished a one-year arrest in 24.8 ±0.9 per cent, *i.e.* in one-fourth of the cases. The results after three years were considerably inferior, with a freedom from symptoms of 16.6 ±0.8 per cent. After five years the number of symptom-free, living patients decreased to 12.9 ±0.9 per cent of the treated patients.

Table VII gives the one-year final results in absolute figures. Out of the 2,529 patients, 627 remained cured for at least one year.

Table VIII shows the three-year results. Out of 2,000 patients treated long enough ago to be included in the report, 330 remained cured for at least three years.

Table IX gives the five-year results in absolute figures. Out of 1,478 patients treated at least five years ago, 190 remained cured.

TABLE VIII

GENERAL SURVEY OF THE THREE-YEAR END-RESULTS 1919–1933 IN ABSOLUTE FIGURES

Location of tumor	Number of cases	Permanent cure
1. Skin	59	23
2. Lips	19	8
3. Orbital region	48	26
4. Auricular region	3	1
5. Inner nose and sinuses	15	2
6. Upper jaw	32	4
7. Oral cavity	87	19
8. Parotid	11	5
9. Epipharynx	31	4
10. Mesopharynx	195	34
11. Hypopharynx	174	18
12. Intrinsic larynx	27	6
13. Branchiogenic tumors	8	—
14. Struma maligna	98	12
15. Breast	332	73
16. Esophagus	169	3
17. Stomach	106	6
18a. Colon	23	3
18b. Rectum	51	5
18c. Anus	4	—
19. Remaining parts of abdomen	26	4
20. Bronchi and lungs	54	—
21. Pleura	1	—
22. Mediastinum	28	3
23. Kidneys	17	—
24. Bladder	12	2
25. Male genitalia	50	8
26. Female genitalia	43	14
27. Hypophysis	21	9
28. Nervous system	22	5
29. Skeleton	28	5
30. Other supporting tissue	19	14
31. Lymph nodes	20	0
32. Metastases only	155	7
33. Miscellaneous	4	1
34. Precancerous lesions	4	3
35. Giant cell tumor	4	4
Total	2,000	330 = 16.5 ±0.8%
Total number minus giant cell tumors, precancerous lesions, lesions of nervous system and hypophysis	1,949	309 = 15.9 ±0.8%

TABLE IX

GENERAL SURVEY OF THE FIVE-YEAR END-RESULTS 1919–1931 IN ABSOLUTE FIGURES

Location of tumor	Number of cases	Permanent cure
1. Skin	50	19
2. Lips	16	8
3. Orbital region	41	20
4. Auricular region	3	1
5. Inner nose and sinuses	9	—
6. Upper jaw	25	4
7. Oral cavity	55	7
8. Parotid	9	2
9. Epipharynx	20	—
10. Mesopharynx	122	14
11. Hypopharynx	116	5
12. Intrinsic larynx	17	4
13. Branchiogenic tumors	7	—
14. Struma maligna	84	10
15. Breast	251	37
16. Esophagus	128	—
17. Stomach	83	4
18a. Colon	15	2
18b. Rectum	29	1
18c. Anus	4	—
19. Remaining parts of abdomen	24	2
20. Bronchi and lungs	36	—
21. Pleura	1	—
22. Mediastinum	24	3
23. Kidneys	16	—
24. Bladder	10	1
25. Male genitalia	36	5
26. Female genitalia	31	8
27. Hypophysis	20	8
28. Nervous system	19	3
29. Skeleton	20	3
30. Other supporting tissue	15	9
31. Lymph nodes	13	—
32. Metastases only	122	4
33. Miscellaneous	2	1
34. Precancerous lesions	3	3
35. Giant cell tumor	2	2
Total	1,478	190 = 12.9 ±0.9%
Total number minus giant cell tumors, precancerous lesions, lesions of nervous system and hypophysis	1,434	174 = 12.1 ±0.9%

This report would be incomplete if we did not mention that the results have improved considerably since 1928. Since 1926 we have owned some radium, and since 1928 we have systematically applied the protracted fractional long time roentgen irradiation as the method of choice.

Table x shows the comparison between

the total results 1919 to 1928 on one side and 1929 to 1935 on the other side for 14 locations of cancer in the body.

The time is too short to go into further details and I therefore limit myself to giving, instead of the absolute figures, only the percentages in Table XI. We see that, after deduction of the borderline malignant tumors and of the esophageal and lung tumors, we had in the former series a one-year freedom from symptoms of 12 per cent, now 30 per cent; a three-year freedom from symptoms of 9 and 19 per cent respectively, and a five-year freedom from symptoms of 8 and 16 per cent respectively. This progress is beyond the statistical error of small numbers; as the mathematical calculation shows, these differences are real.

The report of our therapeutic accomplishments would not be complete without mentioning also the palliative effects. It is more difficult to judge the palliative results than the cures. In order to obtain a judgment which can be expressed in figures, we have calculated the mean survival time of all palliatively treated patients, after deduction of the cured patients. We have furthermore expressed in percentages the improvement shown in the freedom from pain, sometimes in the subjective and objective well being of the patient and in his efficiency. We have considered as favorable palliative effects only those which have shown a marked improvement for at least two months or in which the disease has remained stationary for at least three months with freedom from subjective symptoms.

Out of our 2,529 patients there were 2,093, or 83 per cent, not cured, after the deduction of the cured patients and of those who died from intercurrent diseases after the

TABLE X

COMPARISON BETWEEN THE TOTAL RESULTS OF 1919–1928 AND 1929–1935 IN ABSOLUTE FIGURES FOR A FEW SELECTED CARCINOMATA

Localisation	1919–1928 Alive and free from symptoms			1919–1935 Alive and free from symptoms		
	1 year	3 years	5 years	1 year	3 years	5 years
2. Lips	6 of 11	5 of 11	5 of 11	9 of 13	3 of 7	3 of 5
5. Inner nose	0 of 3	0 of 3	0 of 3	4 of 18	2 of 12	0 of 6
6. Upper jaw	3 of 20	2 of 20	2 of 20	4 of 18	2 of 12	2 of 5
7. Oral cavity	7 of 39	5 of 39	5 of 39	29 of 76	14 of 48	2 of 16
9. Epipharynx	0 of 15	0 of 15	0 of 15	11 of 26	4 of 16	0 of 5
10. Mesopharynx	9 of 62	5 of 62	3 of 62	59 of 190	29 of 133	11 of 60
11. Hypopharynx	0 of 47	0 of 47	0 of 47	51 of 192	18 of 127	5 of 69
12. Intrinsic larynx	0 of 3	0 of 3	0 of 3	13 of 33	6 of 24	4 of 14
14. Struma maligna	6 of 61	6 of 61	6 of 61	8 of 51	6 of 37	4 of 23
16. Esophagus	0 of 29	0 of 29	0 of 29	4 of 219	3 of 140	0 of 99
20. Lungs	0 of 22	0 of 22	0 of 22	1 of 47	0 of 32	0 of 14
22. Mediastinum	2 of 22	2 of 22	2 of 22	3 of 11	1 of 6	1 of 2
27. Hypophysis	5 of 15	5 of 15	5 of 15	7 of 11	4 of 6	3 of 5
28. Nervous system	2 of 10	2 of 10	2 of 10	4 of 17	3 of 12	1 of 9
A. Total	40 of 359	32 of 359	30 of 359	207 of 922	95 of 612	36 of 332
B. Total minus tumors of hypophysis and nervous system	33 of 334	25 of 334	23 of 334	196 of 894	82 of 594	32 of 318
C. Total minus slightly malignant tumors and those of esophagus and lungs	33 of 283	25 of 283	23 of 283	191 of 628	79 of 422	32 of 205

three-year period had elapsed. Out of these 2,093 non-cured patients we have accomplished favorable palliative results in 1,142, or 54 per cent. The mean survival time of the patients who died from the disease was 11.5 months (see Table XII).

If we now summarize the total radiotherapeutic results, *i.e.* the cures as well as the favorable palliative effects, *we have accomplished a favorable therapeutic result in 1,769 out of the 2,529 patients, or in 70 per cent.*

This result is not as discouraging as is generally considered by the laity. Certainly the number of cancer cures is small, but as long as we have no specific therapy for cancer we should not underestimate the palliation accomplished. The situation is similar to that in most internal diseases. The internist can accomplish only palliative effects in a case of damage to the heart muscle. He cannot restore the destroyed structures and he cannot give the patient a new heart. Yet no one doubts that the work of the internist is important and useful. The radiotherapist can also demand this acknowledgment.

TABLE XI

COMPARISON BETWEEN THE TOTAL RESULTS OF 1919–1928 AND 1929–1935 IN PER CENT FOR A FEW SELECTED CARCINOMATA

Localisation	1919–1928 Alive and free from symptoms			1929–1935 Alive and free from symptoms		
	1 year	3 years	5 years	1 year	3 years	5 years
	In per cent					
2. Lips	54	45	45	69	42	60
5. Inner nose	0	0	0	19	13	0
6. Upper jaw	15	10	10	22	17	40
7. Oral cavity	18	13	13	38	29	13
9. Epipharynx	0	0	0	42	25	0
10. Mesopharynx	14	8	5	31	22	18
11. Hypopharynx	0	0	0	26	14	7
12. Intrinsic larynx	0	0	0	36	25	28
14. Struma maligna	10	10	10	16	16	17
16. Esophagus	0	0	0	2	2	0
20. Lungs	0	0	0	2	0	0
22. Mediastinum	9	9	9	3	17	50
27. Hypophysis	33	33	33	64	67	60
28. Nervous system	20	20	20	24	25	11
Total	11	9	8	22	16	11
Total minus tumors of hypophysis and nervous system	10	8	7	22	14	10
Total minus slightly malignant tumors and those of esophagus and lungs	12	9	8	30	19	16

This concludes my report. The results shown could only be accomplished in an independent, clinical in-patient department, with a radiotherapeutic clinic. The radiotherapeutic technician must develop himself into a radiotherapeutic clinician. If and when this requirement is fulfilled, the further progress of the radiotherapeutic fight against cancer depends mainly on early recognition, early admission and early treatment.

TABLE XII

REVIEW OF THE PALLIATIVE RESULTS OF 1919–1935 OBTAINED IN CASES WHO DIED FROM CANCER AND OF THOSE WHO DIED FROM AN INTERCURRENT DISEASE WITHIN THE THREE-YEAR PERIOD

Location of tumor	Number of cases	Number of those not cured	Palliation obtained absolute in per cent	Mean survival period of those who died in months
1. Skin	75	41	22 = 54	13.4
2. Lips	24	11	5 = 45	15.4
3. Orbital region	54	25	18 = 72	19.5
4. Auricular region	9	4	2 = 50	8.0
5. Inner nose and sinuses	21	18	11 = 61	10.7
6. Upper jaw	38	34	16 = 47	10.1
7. Oral cavity	115	86	43 = 50	9.4
8. Parotid	14	8	4 = 50	20.1
9. Epipharynx	41	32	18 = 56	10.8
10. Mesopharynx	252	206	128 = 862	10.4
11. Hypopharynx	239	208	124 = 60	8.3
12. Intrinsic larynx	36	27	15 = 56	9.1
13. Branchiogenic tumors	11	10	3 = 30	5.7
14. Struma maligna	112	96	43 = 45	8.0
15. Breast	403	316	222 = 70	21.6
16. Esophagus	248	245	148 = 60	6.0
17. Stomach	110	103	36 = 35	7.7
18a. Colon	27	23	10 = 43	10.5
18b. Rectum	61	57	24 = 42	10.7
18c. Anus	5	4	3 = 75	16.7
19. Remaining parts of abdomen	28	25	10 = 40	13.2
20. Bronchi and lungs	69	68	15 = 22	4.4
21. Pleura	2	2	1 = 50	2.3
22. Mediastinum	33	29	11 = 38	8.9
23. Kidneys	18	18	5 = 28	7.3
24. Bladder	15	14	6 = 43	9.5
25. Male genitalia	60	49	30 = 61	12.1
26. Female genitalia	61	42	22 = 52	12.6
27. Hypophysis	26	15	9 = 60	33.8
28. Nervous system	27	21	13 = 62	15.0
29. Skeleton	36	31	21 = 68	9.8
30. Other supporting tissue	26	13	9 = 69	32.6
31. Lymph nodes	29	26	11 = 42	8.0
32. Metastases only	188	180	81 = 45	11.3
33. Miscellaneous	4	3	3 = 100	34.5
34. Precancerous lesions	6	3*	— —	—
35. Giant cell tumors	6	—	— —	—
Total	2,529	2,093 = 82.8 ± 0.7%	1,142 = 54.5 ± 1.1%	11.5
Total number minus giant cell tumors, precancerous lesions, lesions of nervous system and hypophysis	2,464	2,054 = 83.4 ± 0.7%	1,120 = 54.5 ± 1.1%	11.4

* All three died from intercurrent disease free from symptoms before the end of the three-year period.

PRINCIPLES GOVERNING ROENTGEN AND RADIUM THERAPY*†

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NO PREVIOUS background existed for the application of roentgen rays and radium at the time when they were introduced into therapy. Everything had to be built from the beginning and the development of the methods was dependent to a large extent on the state of technical facilities. Nor was this the only reason that the development of radiotherapy in various countries took different ways in spite of the many connections which were made possible through meetings and the exchange of ideas in scientific journals. Some institutions had the advantage of collecting experience because of an abundant material or they found new and successful ways, thanks to the initiative of their directors. Thus centers of radiation therapy formed with special methods favored by each of them. The directors of these institutions are in most places still the same and we have to thank them for the development of these methods.

In the meantime a new generation is growing up which did not take part in the development of the radiation procedures which were worked out at various centers of the old and new world. This generation has no prejudice against any of them and wants to compare and evaluate them critically in order to apply the most suitable method themselves. Many of these young physicians visit these large centers of radiotherapy whose names are known all over the world. They note that the various places apply methods which often differ, and in very important points. What they need are standards by which an evaluation can be made. The attempt to gain such standards and with them the basis for the foundation for a general pathology of radiation effects shall be made during a course of four lectures which I have the honor to present during this meeting in accordance with the request of our president. I want to relate briefly some of the problems which are to be discussed during that course.

The best standard by which to evaluate an irradiation method is the result obtained. The reason that some institutions are developing beyond local note and by their increasing reputation attracting students who wish to apply their methods is that these institutions have obtained noteworthy results. But when one is dealing with the results of different institutions one finds that these results obtained by different methods are hardly comparable. As far as a comparison can be made, it is noteworthy that the effects are strikingly similar in spite of great differences in the methods used. One may draw various conclusions from such an observation. A conclusion frequently made is that only a fraction of the tumors can be influenced favorably by irradiation, and that the technique used for this radiosensitive group is not of great importance. This conception is pessimistic as it leaves little hope to enlarge the range of radiation therapy by improving the methods of irradiation. A more optimistic conception is that various irradiation procedures can be suitable, but each one for only a certain proportion of cases. One ought, then, to be able to increase the total number of cures if evidence available could be obtained to select the optimum procedure of treatment for each single case, which presumably is not always the same. There arises then the question whether one ought to individualize in the application of the treatment, and in what way, in order to do justice to each case. This question can be answered only on the basis of an analysis

* From the Radiation Institute, St. Georg Hospital, Hamburg. Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.
† Translated from the German by Dr. E. A. Pohle, University of Wisconsin, Madison, Wisconsin.

of the various irradiation methods according to the significance of their essential factors.

The factors that characterize the various irradiation methods are interrelated, We see that at once when we consider only the most important factor of irradiation procedures, the absolute order of magnitude of the dose. Then if various irradiation methods are to be compared regarding the dosages applied, the difficulty arises at once that one cannot simply compare two physically equally large dosages. Physically equally large doses may have entirely different values according to their time and spatial distribution. Thus the question arises of the influence of the time and spatial relations in irradiation on the effect of a certain dose upon the irradiated organism, a problem which has been investigated largely during recent years. The systematic review of this material clarifies many questions remarkably.

A problem which has not yet been solved concerns the influence of the quality of radiation on the degree and the mechanism of the therapeutic effects. This has attracted more interest during recent years as engineers designed and constructed transformers and tubes with potentials up to one million volts. The answer whether this supervoltage therapy has a practical significance can be given only after a longer period of observation. It seems, however, that by using 600–800 kv. a more favorable relation of the surface and depth effects would be obtained. This is due to the physical properties of the rays. Apparently their application offers advantages already for this reason, advantages which are important even if one cannot adhere to the conception of a fundamental difference in the action of these two kinds of rays. The assumption of the fundamental superiority of short wave radiation is based on the experiences of numerous institutions which had the opportunity to compare the clinical action of roentgen rays and radium, and discovered the therapeutic superiority of radium. But it cannot be overlooked that with the progress in the application of roentgen rays, the results to be obtained by roentgen rays became improved. It even appears that, if the conditions under which roentgen rays and radium act are similar, noticeable differences in their effects are no longer detectable. In the clinical application differences will always remain in the methods under which roentgen rays or radium may be applied. These differences are due to the forms in which these two radiant energies are at our disposal for therapeutic application. This holds for the time as well as for the spatial conditions of application. This alone gives the roentgen rays and the radium their own indications which, in my opinion, will be maintained for some time to come.

The most clear-cut problem of radiotherapy is possibly the relation between effective dose and tolerated dose.* If it is the primary task of radiotherapy to be effective without doing harm, the difference between effective and harmful dose has great significance, and is important for the avoidance of harmful radiation effects. In the recognition of these relationships we passed through several stages: While we thought at the beginning that there was a constant relation between effective and harmful doses for all tumors or at least for all cancers, we soon recognized that a uniform relation between tumor-killing dose and tissue-tolerance dose could not be established due to great variations in the absolute radiosensitivity of tumors of different origin, different histological structure, and different maturity and different size.

Thus the range of radiation therapy is limited from the beginning as being restricted to cases in which the radiosensitivity of the tumor tissues is noticeably higher than that of the surrounding connective tissue. Radiosensitivity of the tumor and tissue tolerance are fixed factors in radiotherapy, just as differences in absorption between the organs of the body are condi-

* "Tolerated dose" in this connection refers to the local dose, which a certain tissue can tolerate, but not to the tolerance dose for the entire organism.

tions necessary for their visualization in roentgen diagnosis. But as the roentgen diagnostician, in spite of the fixed differences in radiolucency, has a wide range of methods for producing more or less contrasty films, so has the therapist the ability, by changes in method, to make the range between effective dose and the limits of tolerance more pronounced, and thus to increase the therapeutic effect.

The clinical experiences as well as the experimental investigations of recent years leave no doubt that the range between effective dose and tolerated dose is decidedly "time-sensitive," or, in other words, that the tolerance of an effective irradiation depends on the time distribution of the dosage. We feel that it is of importance for the appreciation of these relations to consider the total effect of an irradiation with the viewpoints of dosage accumulation and recovery.

The range between effective dose and tolerated dose is also decidedly "space-sensitive," or, in other words, the volume of the irradiated tissue is important for the relation between dose and dose effect. This space-sensitivity of the dosage effect is present in a double sense. For one thing, practical experience leaves no doubt that large doses are tolerated better when they are applied to a small volume. It is believed that not only does the general reaction depend on the size of the irradiated volume but also that an irradiated tissue recovers the more easily from the damage the more limited the area which has been penetrated by the rays. The immediate damaging effect of the rays on the cells which is proved by the well-known degenerative histological processes, seems to be independent of the size of the irradiated volume. The ability of the tissue to regenerate increases, however, with the decrease of the irradiated volume. Thus we formulate the experience that by limiting the irradiated volume, tissue can tolerate doses which would surely lead to severe damage if applied to a larger field.

It is quite different, however—and here enters a second factor in the consideration of the influence of the volume on the effect of the dose—when the irradiated region becomes so large that one has to speak of general body irradiation. Under those circumstances the regression of radiosensitive tumors seems to follow different laws than we know from the local irradiation. At least there is no other explanation if one reads the reports of Mallet in Paris who saw remarkable results in a number of cases with generalized tumors treated by general irradiation with doses of 50–100 r which in local application would never have led to similar regressions.

After all, we all know and can observe again and again that small nodules of a tumor of a certain type under otherwise equal conditions respond better than an extensive area involved with an infiltrating neoplasm. If we compare the last two experiences they perhaps make more understandable the effects of prophylactic irradiation in which comparatively large areas are irradiated in order to reach minute nests of tumor cells. Prophylactic postoperative irradiations are, as can be proved statistically, effective after doses the absolute size of which would not be sufficient to dissolve a large manifest tumor nodule.

All biological rules established in this way are statistical mean values, as far as one is dealing with numerical relations, as for instance, the relation between effective dose and tolerated dose. They are not binding for the single case because they do not account for the fluctuations of all biological properties. Even if we view a very limited tumor species and consider all well known factors influencing the radiosensitivity, great individual differences remain between the dosages which lead to a cure. Thus, other properties of the tumors, still unknown, must be of importance for the radiosensitivity.

Observations on a very limited tumor species, such as the epitheliomas of the skin, revealed that the radiosensitivity is not sharply defined even in the same tumor

species and under similar clinical conditions. Miescher in the small skin cancroids did not find a strictly defined dose limit below which all tumors remained uncured and above which all tumors disappeared, but he found a percentage of cures increasing proportionally to the dosage. The increase of cures parallel with the dose occurred graphically in a characteristic S-shaped curve from the slope of which one can conclude that the radiosensitivity of cancer of the skin varies according to the laws of normal variability with rather wide scatter of the limits of sensitivity of almost 1:3. The same holds for tissue tolerance. The latter is contrary to the usual line of thought which permits at the most a range of fluctuation of 20 per cent, varying to a much larger extent.

A study of the late skin changes of patients, who had been irradiated in our institution three to five years ago according to the protracted fractional dose method, showed that the limit in the occurrence of telangiectases has a wide range of at least 1:2.2. One can suppose that the same holds also for necrosis, that form of damage which is always beyond the limits of tolerance. The fact that effective doses and tolerated doses are not strictly limited but have larger ranges has the consequence that it is impossible, even if the mean value of the tumor-killing and the mean value of the tolerance dose are far apart, to apply a dose which is effective in each case without harming a smaller or greater number of cases. It is not justified to decrease the dosage, in consideration of the above facts, to such an extent that no harm can be done under any circumstances, just as it is not justified to limit operations to cases which show no operative mortality. But for the operation, as well as for the irradiation, it has to be carefully considered whether the possible gain is worth the risk. Closer study reveals that for tumors with a primary curability of 30 to 50 per cent a slight passing of the lower limit of the tolerance range is justified because considerable increase of the chances for cure are obtained with slight increase of the risk. Thus, this statistical way of observation is not only a more or less interesting speculation but also has practical consequences for our actions. It gives us more security in our indications but at the same time we hesitate to overestimate the importance of damage in a single case in the judgment of the methods of irradiation as a whole. I stated at the beginning that it is our task to establish standards for an evaluation of the irradiation methods of today, and it is just as important to avoid wrong standards.

Because of lack of time, the ideas which may serve as a foundation for a system of general radiation pathology can be sketched only briefly. I summarize them as follows:

The knowledge of the dose, after consideration of the relations between physical dose and biological effects.

The knowledge of the influence of temporal and spatial conditions in radiation therapy.

The estimation of radiosensitivity of tumors in relation to the tolerance of the tissues.

The consideration of the variation of the radiosensitivity of the tumor and of the normal tissue for outlining the indications applying in the individual case.

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THE TEMPERATURE COEFFICIENT OF THE EFFECT OF RADIATION ON PROTEINS AND ITS RELATION TO INJURY OF THE LIVING CELL*

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THE effect produced in proteins as the result of the absorption of radiant energy is an important factor in all radiobiological problems, since the properties of living matter are so dependent on its protein elements.

The chemical and physicochemical changes produced by radiation in proteins and amino-acids have been summarized in several recent reviews.[3,7,21] It has long been recognized that the effects observed depend on the nature of the protein, the electrolytes present, the hydrogen ion concentration of the protein solution and the wave length of the radiation. Also, though it has not been emphasized sufficiently, the observed effects depend on the temperature of the protein solutions subsequent to irradiation. The object of this paper is to bring out the importance of the temperature coefficient of radiation effects and its probable bearing on radiological problems.

The most striking and important change produced in all protein solutions when irradiated, whether the protein is a globulin or an albumin, whether it is positively or negatively charged, is a change in solubility of the protein molecule which we call denaturation. This change may be brought about by various agencies, one of which is heat, another radiation. It is unimolecular in nature and appears to be associated with some internal physical or chemical change within the structure of each protein unit. The denaturation produced by radiation and that produced by heat differ in some respects,[20] but all types of denaturation decrease the solubility of proteins so that they are more readily precipitated. Although it has been stated[2] that heat denaturation may be reversible under certain conditions, and although the recovery taking place after irradiation in the living cell points to some degree of reversibility, radiation denaturation is in general irreversible and so alters the proteins that they can no longer act as normal constituents of the living cell. It is therefore an effect of primary importance in considering the lethal effect of radiation on tissues.

The steps involved in the process of radiation denaturation and the importance of the temperature coefficient of these radiation effects have been studied in some detail in the case of ultraviolet radiation but have hardly been touched upon in the case of roentgen and radium rays. Some recent work on the effect of ultraviolet radiation on proteins will therefore be summarized and discussed in view of the possibility that similar experiments on the changes produced by shorter wave lengths may lead to interesting results both in laboratory investigations and in clinical practice.

The Effect of Ultraviolet Radiation on Salt-free Albumin. In a recent paper by the author[4] it was found that, by controlling the temperature at which denaturation and subsequent flocculation took place, a quantitative analysis of the process could be made and coagulation was found to take place in three steps. In this investigation isoelectric egg albumin solutions were irradiated on ice at 4° C., heated after irradiation in constant temperature baths, and the degree of aggregation was measured by the intensity of the Tyndall beam from the opalescent solutions. The intensity was read in apparent foot-candles by means of a Macbeth illuminometer, as shown in Figure 1, and under certain specified conditions gives a quantitative measure of the

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

concentration of aggregated material. The source of radiation was a quartz mercury arc.

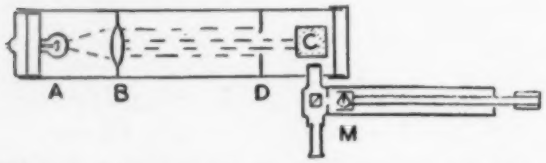

Fig. 1. Diagram of Tyndall meter. A = lamp, B = lens, D = diaphragm, C = cell (2 cm. square), M = Macbeth illuminometer.

If salt-free albumin solutions are irradiated on ice at the isoelectric point, there is no visible change and no increase in the intensity of the Tyndall beam although light denaturation has occurred, as can be shown by the smell and color of the solutions and by their subsequent behavior.

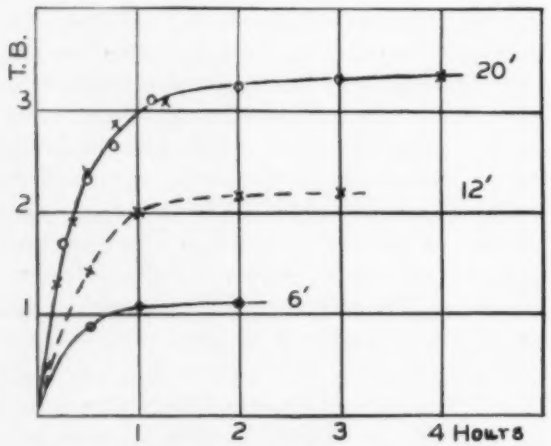

Fig. 2. Increase in Tyndall beam on immersion in bath at 40° C., for solutions irradiated six, twelve, and twenty minutes at 6 inches from the arc. (x = results for solutions irradiated at 4° C. and o for solutions irradiated at 14° C.). Ordinates = Tyndall beam in apparent foot-candles. Abscissae = time of immersion in bath.

If, after irradiation at 4° C., these isoelectric solutions are brought to 40° C. for an hour and a half, there is an increase in opalescence, as shown in Figure 2. In this figure the values given by x on the curves represent solutions irradiated at 4°C. and those given by o represent solutions irradiated at 14° C. As the subsequent rate of coagulation at 40° C. is the same for both lots, the temperature coefficient of the initial change produced by irradiation is 1.

The rate at which a certain degree of opalescence was reached when irradiated solutions were brought to 30° C. and 40° C. showed that the temperature coefficient of this second step as measured by Vel 40° C./Vel 30° C. is 10+ This is shown in Figure 3, and it is interesting to note here how slowly the second step, which is a heat change in the light denatured molecules, takes place at 20° C. In the few papers where the temperature coefficient of the effect of roentgen rays has been studied, the temperatures used usually fall below 25° C. where the rate of the heat change is too slow to be easily measurable.

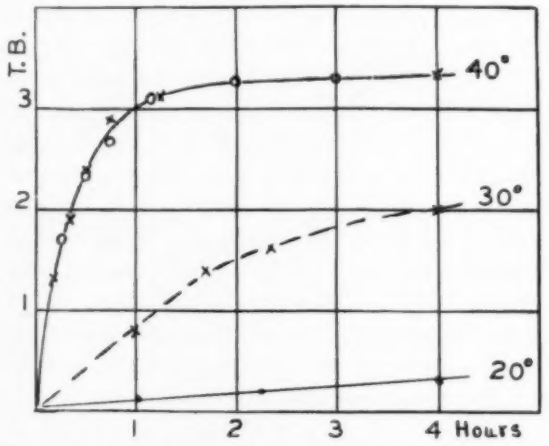

Fig. 3. Increase in Tyndall beam in solutions irradiated for twenty minutes at 6 inches on immersion in baths at 20°, 30° and 40° C. (x = solutions irradiated at 4° C. and o = solutions irradiated at 14° C.). Ordinates = Tyndall beam in apparent foot-candles. Abscissae = time of immersion.

If albumin solutions are irradiated at 4° C., at a pH removed from the isoelectric point, and then heated to 40° C., there is no coagulation, but if these solutions are then brought to the isoelectric point flocculation occurs.

The results therefore can be summarized in the following way.

(a) Albumin solutions irradiated at 0° C., denaturation but no flocculation.

(b) Heated to moderate temperature (40° C. for 1½ hours) after irradiation,

flocculation near isoelectric point, solutions clear if more acid or alkaline.

(c) These more acid or alkaline solutions flocculate if then brought to the isoelectric point.

The conclusion arrived at is that the coagulation of salt-free albumin by ultraviolet radiation involves three distinct processes. The first step, the light denaturation of the protein molecule, is a physical change which occurs at any temperature or hydrogen ion concentration. It is unimolecular, has a temperature coefficient equal to 1 and, though it occurs when the protein is irradiated at 0° C., it is not followed by flocculation until the irradiated protein is heated to a moderate temperature. The second step is a chemical reaction between the light denatured molecule and water with the high temperature coefficient of 10. This may be similar to heat denaturation but occurs at a much lower temperature. The third step is the flocculation of the light and heat denatured molecules to form a visible coagulum. This is a physical change which occurs only at the isoelectric point in salt-free protein solutions.

The Effect of Ultraviolet Radiation on Protein Solutions in the Presence of Salts. The presence of salts extends the coagulation range somewhat. Calcium salts have a greater effect than sodium and potassium salts and when they are present egg albumin shows opalescence up to pH 6.0 after irradiation at 4° C. and subsequent heating to 40° C. As in the case of isoelectric, salt-free albumin the temperature coefficient of the initial light denaturation is equal to 1 and that of the second step produced by moderate heat after irradiation[6] is between 8 and 10.

Similar experiments were performed with extracts of lens protein in sodium, potassium, and calcium chloride solutions.[5] After irradiation at 4° C., at the pH of the lens (7.0–7.2), there was no opalescence in any of the extracts. When the irradiated solutions were heated to 40° C. for one hour, opalescence developed in extracts containing calcium or magnesium salts, a concentration of 0.05 per cent of calcium chloride being sufficient to produce a definite effect. This development of opalescence, after irradiation and subsequent heating to body temperature, may be a factor in certain forms of cataract. The temperature coefficient of the initial step of light denaturation was found to be 1.13 and that of the second step or heat change was found to be 11.4. The results for the temperature coefficient in the presence of salts were less exact and satisfactory than those with isoelectric salt-free albumin, but it is evident that it may be said in general of protein solutions, whether salts are present or not, that, although radiation denaturation takes place at 0° C., irradiation must be followed by a rise in temperature before flocculation takes place. This flocculation takes place only at the isoelectric point, in salt-free solutions, but, if calcium or magnesium salts are present, coagulation may take place at the pH at which cells and tissues are ordinarily found.

Temperature Coefficient of the Lethal Action of Ultraviolet Radiation on Cells. The conclusion given above suggests interesting speculations in regard to the lethal action of radiation on cells and microorganisms. Is the primary change of radiation denaturation sufficient to kill the cell or must it be followed by the second step, the temperature change producing coagulation, before lethal effects occur? If the latter, then irradiation would only be effective in producing a lethal action on cells if combined with, or followed by, heating to a moderate temperature.

Published experiments on the bactericidal effects of radiation give no information on this point as the cultures are always incubated at 37° C., and therefore both the first and second steps in the process invariably occur.

Some experiments were carried out in order to test this point. Paramecia were irradiated in water at 4° C. and subsequently incubated in hay infusion at 25° C. and 33° C. Direct observation of organisms

after irradiation at 4° C. for five minutes at 18 inches from a Hanovia arc showed that some were dead as the result of rupture of the membrane. All organisms were killed at once by six to seven minutes' irradiation at 4° C. under these conditions. Organisms were injured so that death occurred inside a day by four to five minutes' exposure to ultraviolet radiation, but the rate of death

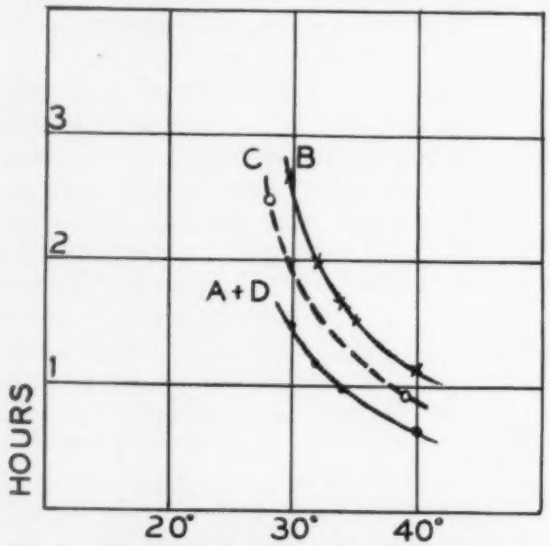

Fig. 4. Latent period of erythema in human skin plotted against temperature (4 subjects).

was the same if they were incubated at 25° C. or 33° C. after exposure. It is apparent, therefore, that microorganisms are killed almost instantly by irradiation due to injury of the cell membrane under conditions in which protein coagulation cannot take place. If a protein change is involved, it is only the initial process of light denaturation. Rentschler,[18] who watched paramecia under the microscope during irradiation, found that the initial effect was a rounding up of the organism probably due to increased permeability and internal pressure.

It is probable, therefore, that the temperature factor is unimportant in the lethal action of irradiation on microorganisms and death is apparently not due to a coagulation of cell proteins, although coagulation subsequently occurs as is shown in photomicrographs of paramecia killed by ultraviolet radiation.

Temperature Coefficient of Erythema. The fact that there is a distinct latent period in the appearance of erythema after exposure to ultraviolet radiation shows that the initial light change must be followed by a secondary change. Recent experiments by the author[6] have shown that the temperature coefficient of the initial light change is approximately 1 as skin irradiated at 22° C. and 35° C. showed the same degree of erythema and the same latent period.

If skin is irradiated at room temperature and then immersed in water baths at 30° C. and 40° C. there is a shorter latent period at the higher temperature and the temperature coefficient is found to be equal to 2.3 (Fig. 4). As this is not the temperature coefficient of the second step in protein coagulation, the changes taking place in the skin that lead to erythema are probably not related to the coagulation of tissue proteins.

It therefore appears that although the injury to the cell membrane produced by irradiation, which leads to the death of microorganisms, has a very low temperature coefficient, the skin change resulting in erythema has a temperature coefficient of approximately 2, and the second step in the coagulation of proteins has a temperature coefficient of approximately 10. And, although the primary biological effect of radiation may always be independent of temperature, these primary changes are usually followed by secondary changes which may have high temperature coefficients. The relation of temperature to the effects produced by roentgen rays and radium has not been investigated thoroughly and an appreciation of the importance of the temperature factor, especially where protein changes are involved, may lead to important advances.

Temperature Coefficient of Coagulation of Proteins by Roentgen Rays and Radium. Several investigators have counted the particles visible under the ultramicroscope in order to follow the denaturation and flocculation produced in proteins by exposure to roentgen rays.

Rajewsky,[16] using this method, exposed egg albumin to roentgen rays at different temperatures, and counted the number of particles photographed under the ultramicroscope. He found a shorter latent period and a greater number of particles when a higher temperature was used. Solutions irradiated at 23° C. and then kept at 60° C. show more aggregation in a shorter time than solutions irradiated and kept after irradiation at 23° C. This indicated that the process of denaturation and coagulation of proteins by roentgen rays and radium has the same three steps that have been found in the case of ultraviolet radiation.

Temperature Coefficient of Roentgen Injury to Cells. Although the lethal effect of ultraviolet radiation on microorganisms has a low temperature coefficient and seems to be related to membrane injury rather than to protein coagulation, it is possible that some of the injuries produced by roentgen rays and radium in cells and tissues may be due to protein changes, in which case it would probably be necessary for the radiation change to be followed by a heat change before injury takes place and the degree of injury would depend to a very large degree on the temperature of the cells after irradiation.

Various workers have shown that the initial change produced by irradiation is practically independent of temperature as one would expect.

Henshaw and Francis[12] exposed wheat seedlings to roentgen rays during germination at different temperatures and found that stopping growth, by lowering the temperature during irradiation, did not change the radiosensitivity. The seedlings were, however, all kept at the same temperature after irradiation.

Redfield and Bright[17] exposed the eggs of *Nereis* to roentgen rays at 0° C. and 25° C. and measured the effect on the thickness of the fertilization membrane. They found a temperature coefficient of 1.1–1.2, but in these experiments the eggs after exposure were all kept at the same temperature so the coefficient relates only to the initial process.

Dubowy[9] found that temperature did not influence the biological action of roentgen rays on the pupae of *Drosophila*. He irradiated the pupae at 4° C. and 25° C. After irradiation they were kept at 25° C. and the number killed was the same in both lots.

Ancel and Vintemberger[1] found no difference in the results when frog eggs or chicken eggs were irradiated at 11° C. and 25° C. and subsequently incubated. Here also the temperature was only controlled during the first step of the process and there is no indication of the influence of temperature subsequent to irradiation where it might be significant.

Packard[15] exposed the eggs of *Drosophila* to roentgen rays at 13°, 23° and 28° C. After irradiation they were incubated at room temperature and the number that hatched were determined. He found greater injury when the eggs were exposed at a higher temperature. Packard also irradiated the eggs at room temperature and then incubated them at 18° C. and 28° C. There was greater injury at the higher temperature. Packard, in these experiments, gives evidence for a temperature coefficient greater than 1 both in the primary and secondary radiation changes. Here the result is complicated by the effect of temperature on division rate, and Packard interpreted his results as evidence for an increased sensitivity of the cell with increased division rate.

Dognon,[8] however, exposed *Ascaris* eggs to roentgen rays and found that, though the segmentation rate reached a maximum at 35° C., the injury produced by irradiation increased with temperature up to 47° C. He found little effect of temperature up to 20° C. and after that a rapidly increasing sensitivity. As the majority of workers have used temperatures below 25° C. their results are less striking than those of Dognon. As the second step in the coagulation of proteins by ultraviolet radiation takes place with almost immeasurable slowness below 25° C., and only becomes rapid in the neighborhood of 40° C., Dognon's results suggest that there is a secondary change involved with a high temperature coeffi-

cient. Dognon interpreted his results to mean that he was dealing with two effects, one independent of temperature (primary process) and one variable with temperature (secondary process) and, although the temperature was controlled only during the irradiation, the results indicate that the injury observed may have been due to protein changes.

The best evidence, however, for the suggestion that the injury of living cells by roentgen rays may be influenced by the temperature subsequent to irradiation is given by Strangeways and Fell.[22] In their experiments they exposed six-day chick embryos to roentgen rays *in ovo*. After a dose of 270 e, followed by incubation *in ovo* at 38° C., mitosis was almost or completely absent and tissue taken from embryos irradiated and incubated for twenty-four hours showed no trace of growth when explanted *in vitro*. If, after a dose of 270 e, the embryos were kept at 5°C. for twenty-four hours degenerative changes were delayed, if not arrested, and tissue fragments showed fair growth with mitosis when cultivated *in vitro*.

It would seem, therefore, that the primary effect of roentgen rays must be followed by a secondary change with a definite temperature coefficient before marked injury occurs. If the secondary change is prevented or delayed, by lowering the temperature after irradiation, injury will be delayed and a certain amount of recovery may take place. If the secondary change is accelerated by increasing the temperature after irradiation, there should be more rapid and more extensive injury. In physiologically inactive test objects, such as protein solutions or dry seeds, the final effect produced by radiation is irreversible. However when cells are functionally active, there is a process of repair which indicates reversibility of the radiation changes and, if the secondary effect can be postponed by low temperature, injury may be largely prevented. It is probable that radiation denaturation would be more readily reversible after exposure to roentgen rays where, owing to the small absorption, the denatured molecules are widely scattered instead of being concentrated in relatively dense layers, as is the case on exposure to easily absorbed ultraviolet radiation.

Clinical Aspects of the Temperature Coefficient of Roentgen Injury. These conclusions should have important clinical bearings and although a number of scattered results have been reported on the combined use of heat and roentgen rays, the experiments were carried out without a clear picture of the rôle played by temperature in radiation changes.

Several investigators have reported that heat will increase the degree of erythema after roentgen exposure. Hawkins,[10] and Hawkins and Clark[11] found that if heat and roentgen rays were applied simultaneously to the skin of a guinea pig, well-marked burns resulted, although the dosage of roentgen rays alone was not sufficient to cause even a mild erythema. In a second series of experiments, areas on the same animal were exposed to suberythema doses of soft roentgen rays, to heat below the critical dose for producing a burn, and to heat and roentgen rays in sequence with various time intervals between the exposures. The only effect of exposure to roentgen rays or heat alone was a slight scaling of the skin after roentgen irradiation. The areas exposed to both roentgen rays and heat developed persistent burns when the exposure to one agent was made within three hours of the other. The results were the same whether roentgen rays or heat was applied first.

Meyer and Mutscheller[13] irradiated patients through a hot water chamber in contact with the skin and found that erythema was produced in a shorter time and with one-third to one-half the usual erythema dose.

The opposite effect, that of cooling the skin during and after roentgen exposure, in order to delay the secondary change and minimize or eliminate skin injury, has not been tried but would be interesting and possibly of clinical value.

Sixteen years ago Rohdenburg and Prime[19] tried the effect of combined radiation and heat on tumors. Fragments of transplantable tumors were exposed to heat and radiation separately, or combined, and then inoculated into mice. It took 120 minutes' exposure to 43° C. and 5 erythema doses of roentgen rays to kill the tumor cells if heat or roentgen rays were given alone. But 3 erythema doses and thirty minutes' exposure to 43° C. produced a lethal effect if both agents were used, no matter which one was applied first. Good results were also obtained by combined heat and roentgen treatment *in vivo*.

More recently Overgaard[14] experimented with Wood's sarcoma on the tail of rats. One group was treated with diathermy alone, another with roentgen rays alone, a third group with diathermy followed the next day by roentgen rays and a fourth group by roentgen rays followed the next day by diathermy. The roentgen-ray dose was 800 r and the temperature was 42° C. for ten minutes. Diathermy alone had no effect, roentgen radiation alone 11.5 per cent healing, diathermy followed by roentgen radiation 22.3 per cent healing, and roentgen radiation followed by diathermy 48.5 per cent healing. By comparison with Hawkins' work one would expect that more striking results would have been obtained if the interval between roentgen radiation and heat had been shorter.

Meyer and Mutscheller[13] found that superficial epithelioma could be treated with combined roentgen rays and heat with good results and a lower dosage than when roentgen rays were used alone. Taylor,[23] however, reported that heating by means of ultra high frequency currents did not sensitize experimental rat tumors to nonlethal doses of radium.

In general, however, the results indicate that heat applied after exposure to roentgen rays will increase the effect of radiation on tissues. This is to be expected from the results reported in the earlier part of this paper on the temperature coefficient of the second step in the radiation changes in proteins and skin tissues. The fact that heat seems also to be effective if applied immediately before radiation suggested the possibility that in the denaturation and coagulation of proteins by ultraviolet radiation the first step (radiation change) and the second step (heat change) might be reversed in order.

Experiments were carried out to test this point both with isoelectric egg albumin and with lens extracts in Ringer's solution to which 0.1 per cent calcium chloride had been added. It was found that the two steps are not reversible. Heat, followed by radiation, does not give the opalescence that is given by irradiation followed by heating. Nevertheless, if the solutions which have been heated before irradiation are then heated after irradiation they show greater opalescence than those which have only been irradiated. Preliminary heating may therefore sensitize proteins to the effect produced by irradiation and subsequent heating. Although the effect of heating before irradiation may not be significant it is very probable that local heating after irradiation will accentuate the effect of all forms of radiation on tissues and local cooling of the skin during and after irradiation may prevent erythema. The clinical results so far obtained bear out this conclusion which is drawn largely from the effects of radiation on proteins and strongly emphasize the importance of the temperature factor in all radiobiological problems.

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Vol. 40, No. 4

CANCER OF THE LARYNX

RESULTS OF ROENTGEN THERAPY AFTER FIVE AND TEN YEARS OF CONTROL*†

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CANCER of the larynx constitutes one of the most instructive types of tumor for the purpose of studying the effects of irradiation on neoplastic disease. In no other part of the body does one encounter the extreme histological varieties, ranging from undifferentiated or slightly differentiated epitheliomas of the mucous membrane type to the differentiated and infiltrating cutaneous type with epithelial pearls. We omit from this discussion such rare tumors of the larynx as sarcoma and adenocarcinoma.

In no other part of the body does one find gathered together, in so small a space, so great a variety of anatomical-pathological forms, varying from small papillary lesions of the mucous membrane and submucosa to lesions which infiltrate the underlying muscle and finally those which destroy the neighboring cartilage and bone.

This diversity in the anatomo-clinical and histological forms of laryngeal cancer results in a highly variable radiocurability. It is without doubt the most variable of all the varieties of cancer.

Cancers of the larynx may be clinically divided into three groups: (1) cancers of the vestibule and ventricular cavity, or supraglottic; (2) cancers of the glottis; (3) cancers of the subglottis.

The supraglottic cancers are of two types: the first, in the neighborhood of the mucosa of the pharynx, are generally epitheliomas of the mucous membrane type, analogous to those of the pharynx, since they arise in the superior part of the vestibule, in a borderline region. They are frequently accompanied by adenopathy. The second type arises in the middle and inferior zone of the vestibule and in the ventricular cavities. These are stratified epitheliomas of the mucous membrane type, arising from a cylindrical metaplastic epithelium. They are more rarely accompanied by adenopathy.

The second localization, that of cancers of the glottis, are generally epitheliomas of the cutaneous type; they are never accompanied by adenopathy.

The cancers of the subglottic localization are of the cutaneous type when they arise a short distance below the cord, in the superior half of the subglottis. They are of the mucous membrane type (metaplastic epitheliomas) when they arise a greater distance from the glottis, from the cylindrical cells of the inferior part of the subglottis.

CLASSIFICATION OF RESULTS

The curve in Chart 1 indicates the proportion of annual cures of epitheliomas of the larynx treated from 1921 to 1932. The curve of the survivors after five years of control is given up to 1932, while the curve of the survivors after ten years of control, which is the lower curve, ends with those cases treated in 1926.

The curve after five years of control shows the great diversity of results throughout the course of successive years. The three peaks of the curve correspond to the three best years.

In 1921, 4 patients in 8 are living after 5 years, or 50 per cent.

In 1926, 9 patients in 17 are living after 5 yaers, or 52 per cent.

In 1932, 6 patients in 9 are living after 5 years, or 66 per cent.

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.
† Translated from the French by Dr. Simeon Cantril, Chicago, Ill.

Between the three years of good results, each separated from the other by four to five years, we have two years of intermediate results:

In 1925, 6 patients in 17 are living after 5 years, or 35 per cent.

In 1931, 2 patients in 7 are living after 5 years, or 28 per cent.

The seven other years have given us variations between 0 and 20 per cent.

The results of 1921 (50 per cent) left us with the hope that the question of cancer of the larynx would be relatively easy to solve. Our hope had as its only excuse our ignorance of the problem. We were in fact convinced at that time that roentgen therapy was a matter of dosage, and we thought there existed a cancericidal dose relatively low for undifferentiated epitheliomas, higher for differentiated epitheliomas. Under these conditions, we thought that if we learned how to save the general tissues, that is, to avoid all local and general accidents, we could probably obtain cures in a high proportion of cancers. On the other hand, the doses which we were led to consider as curative were particularly easy to attain or even to exceed in the region of the larynx, because of its superficial position.

But we were rapidly brought back to more just conceptions, because the year 1922 left us no survivors of five years among 11 patients treated, and the year 1924 gave us only 8 per cent.

In 1926, the survivors of five years again being numerous (52 per cent), we once more had some hope of maintaining the good results. But in the years from 1927 to 1930, the survivors of five years were again more rare.

In the year 1932, we had 66 per cent survivors of five years, but we no longer held any illusions. The question of cancer of the larynx was much more complex than we had thought, and we began to understand that progress would be slow. In effect, the curve demonstrates that, when the three favorable years are omitted, there exists only a slight progress in the results of the less favorable years.

No cancer has given us annual statistics as irregular as those of cancer of the larynx.

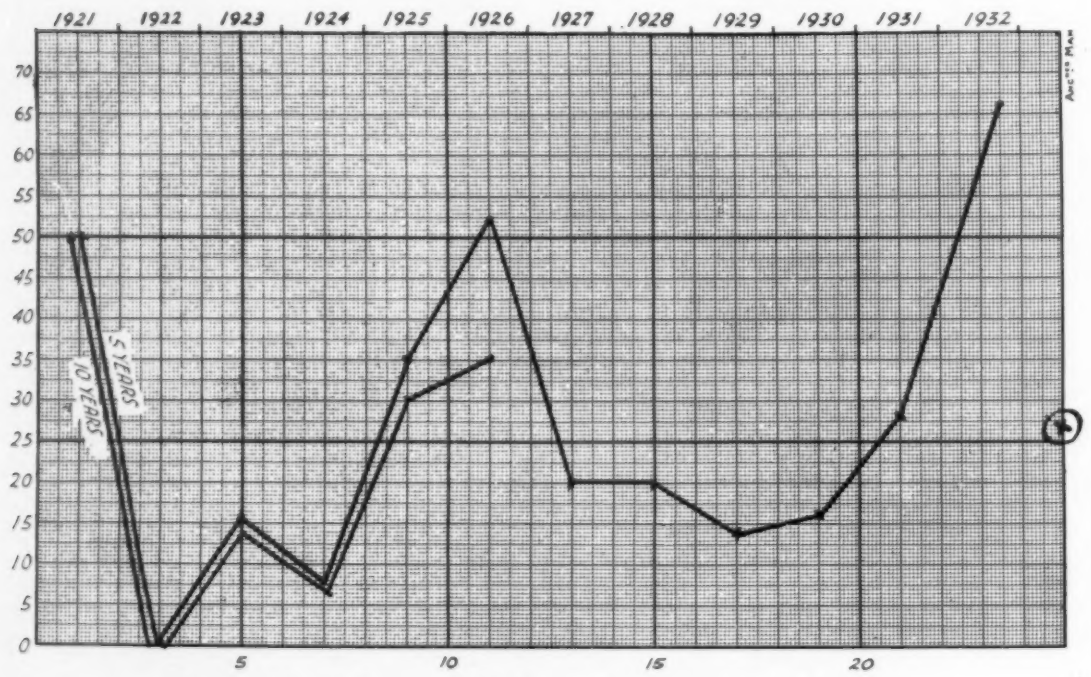

CHART 1. Cases of cancer of the larynx. Five and ten years of control.

If we consider an epithelioma very close, and consequently treated in an analogous manner, namely that of the hypopharynx, we see that the proportion of cures for the patients treated from 1921 to 1929 is low, but has not varied widely. The average number of survivors of five years is 10 to 12 per cent. The best years have not exceeded 16 per cent, and the least favorable years have not fallen below 5 per cent; the variation in results is thus 11 per cent.

In the epitheliomas of the larynx, the average of five-year survivors from 1921 to 1932 is 27 per cent; the best year reached 66 per cent, the worst year left us no patients surviving among 11 treated; the variation is thus 66 per cent. The variation of the results in laryngeal cancer is six times greater than for pharyngeal cancer, because the diversity of types is much greater in the larynx. In the epitheliomas of the pharynx, the histological forms vary only slightly. They are always epitheliomas more or less differentiated, but of mucous membrane type, and almost always accompanied by adenopathy.

TABLE I

CASES OF CANCER OF THE LARYNX—FIVE AND TEN YEARS OF CONTROL

Five Years						
1921	1922	1923	1924	1925	1926	1927
4 out of 8	0 out of 11	2 out of 12	1 out of 12	6 out of 17	9 out of 17	2 out of 10
50%	0%	16%	8%	35%	52%	20%
1928	1929	1930	1931	1932	Average	
4 out of 20	1 out of 7	2 out of 12	2 out of 7	6 out of 9	39 out of 142	
20%	14%	16%	28%	66%	27%	
Ten Years						
1921	1922	1923	1924	1925	1926	
4 out of 8	0 out of 11	2 out of 12	1 out of 12	5 out of 17	6 out of 17	
50%	0%	16%	8%	30%	35%	

In addition to the types of cancer of the larynx as a primary cause of success or failure, there necessarily exist causes inherent in the methods of treatment.

CAUSES OF SUCCESS OR FAILURE INHERENT IN TREATMENT

In 1921, 1922 and 1923, we thought that the distribution of a sufficiently high total dose would give us an adequate chance to destroy neoplasms of the larynx. In 1921 we attempted the production of the radio-epidermitis of Regaud and Nogier immediately over the lesion, namely, on the side of the lesion only, in order to assure a sufficient effect on the neoplastic cells. At the same time we produced a very severe radio-epithelitis of the mucosae. The treatments were given in seventeen days on an average. Of the 4 cases cured, 3 were undifferentiated forms, of which 1 had a tracheotomy and invasion of the thyroid cartilage, which was partially destroyed. The fourth case was somewhat more differentiated. The doses given were about 6,500 to 7,000 r measured on the skin, over two fields, right and left, of 40 to 50 sq. cm., with a higher total dose on the side of the lesion, *and the daily doses were higher as the end of treatment was reached*, when they attained 700 r the last three to four days.

In 1922, 11 patients were treated, with higher doses given in a shorter time, 7,500 r in ten to twelve days. Three patients only survived more than three years, and none survived five years; 1 died of cardiac disease, 1 of cirrhosis, and a third of amebic enteritis.

In 1923, the doses were increased still further, up to 8,000 r, and distributed over an analogous time, with daily doses necessarily very high—600 to 700 r. There has been only one survivor of five years from this method, and this was a patient with an

undifferentiated epithelioma of the ventricular cavity, who is still living, but has very marked changes in the skin.

Seeing that high total doses could not be tolerated in a short time, we then gave them, at the end of 1923 and in 1924, *in two series of treatments*, divided by twelve to fifteen days. The first series was given from the first to tenth day, producing a radioepithelitis on the thirteenth day; the second series was given after the healing of the first radioepithelitis, namely, after the twenty-second day, which produced a second radioepithelitis, accompanied by a radioepidermitis, both appearing toward the twenty-eighth day. We thought that two successive radioepithelites ought to guarantee sterilization.

These high total doses produced still further modifications of the vascular connective tissue, despite their division in two series. Among the 10 patients thus treated, 2 only remained cured. But one of these was a differentiated epithelioma of cutaneous type, with complete fixation of the hemilarynx. This was the first case of this type to be cured.

At the end of the year 1924 and the beginning of 1925, because of the continued production of too severe reactions, the treatments were prolonged over forty, forty-five or fifty days, because we were not yet free from the idea of high total doses for all cancers. In the presence of the bad results obtained, we decided to again lower the doses and the time of treatment, at least in the cases which seemed to us would benefit by a condensed time of treatment.

Thus at the end of 1925 and in the course of 1926, the doses for certain patients were again reduced to 6,000 to 6,500 r, given in twelve to seventeen days. This was the period of good results—35 to 52 per cent. For other patients, the doses were 7,000 r given in thirty to forty days, which produced several satisfactory results.

In 1927 the treatment times were maintained at thirty to forty days (20 per cent). Their duration was again reduced in 1928 and 1929, but without sufficient reduction in the doses, which again gave us poor results (20 and 14 per cent).

The same doses were again distributed over a longer time in 1930 and 1931 (16 and 28 per cent).

In 1932, the treatment times reached fifty to sixty days for total doses of 8,000 to 9,000 r, with very good results. But the treatments, strictly speaking, *were preceded by a period of preparation*, which varied between ten and thirty days for doses of 1,000 to 2,000 r, the preparation made by very low daily doses of about 100 r, so that the really active treatment, destroying the more differentiated cells, did not exceed thirty to forty days in duration, with doses of 6,500 to 7,000 r.

If now we examine the curve of results not only after five years, but after ten years, we see that among the patients cured in the years 1921, 1922, 1923, and 1924, we have had no deaths. The 7 patients who lived for five years are still living after ten years. But it is otherwise for the patients treated in 1925 and 1926: 4 patients died after five years. One of these is of no interest—treated in 1925, he died in 1934, without recurrence, at the age of seventy-nine, and after nine years' survival. But 3 patients treated in 1926 died of late recurrence at about sixty years of age. One of these died in the sixth year, and two during the eighth year. These 3 patients were treated in fifteen, sixteen and twenty-one days; they received the same total dose, 6,000 r, and were treated in a similar manner. *They received high daily doses of 600 to 700 r during the first three to four days of treatment only, after which these high doses were reduced to 300 r.* The examination of the observations on these patients, and on many others, has led us to think that the reduction of the daily doses after several days of treatment was a frequent cause of failure in cancers moderately differentiated. In other words, this reduction in the daily doses at the end of a condensed treatment constitutes a poor distribution of the energy in time, while *the increase of the daily doses at the end of a condensed treatment has*

in general been more favorable. We thus see the appearance of three factors in the treatment of cancer of the larynx: *the total dose, the daily dose, and the moment of distribution of certain daily doses.* We see, moreover, that we have always hesitated between quite high total doses, given in general over a long time, with relatively low daily doses, and somewhat lower total doses given in a shorter time with high daily doses. We were justly hesitant, because we knew that the two methods were sometimes efficacious, sometimes inefficacious, but we did not know how to apply them correctly.

CLASSIFICATION OF CANCERS OF THE LARYNX ACCORDING TO THE RESULTS OF ROENTGEN THERAPY

The study of all the cases treated permits us to point out the errors committed. The first was to increase the total doses excessively when the treatment was given in a short time. The second was to consider that the same treatment could be applied to cancers of a different nature. The third was not to understand that the alternation of good and bad years was due in a large measure to the great difference in the proportion of favorable and unfavorable histological types.

We now know that cancers of undifferentiated cells, extremely fragile, can be cured by all varieties of irradiation, while cancers of very differentiated and infiltrating cells are only exceptionally cured. The former benefit as well from high total doses given over a long time, as from relatively low doses given over a shorter time. In the differentiated cancers, the increasing of the total dose does not always aid in producing a cure, but can, on the contrary, as we shall see further on, definitely arrest the neoplastic involution.

The results obtained by roentgen therapy lead to an excellent practical division of cancers of the larynx. The mobility of the laryngeal muscles or, on the contrary, the total absence of mobility of these muscles and of the arytenoid cartilage, permits one to form an opinion as to the curability of cancer of the larynx.

If, for example, a hemilarynx is totally immobile, if the muscles are infiltrated by the neoplasm, if the arytenoid cartilage is totally fixed, the radiosensitivity is low, the possibility of cure is reduced. One thus has generally a very differentiated cancer. If, on the contrary, the muscles remain free, if the cords, bands, and arytenoid cartilages have only a slightly reduced mobility, then even if the tumor is voluminous, necessitating a tracheotomy, and has destroyed part of the thyroid cartilage, it is possible to obtain a cure in a great many such cases. These are, in general, cancers formed of only slightly differentiated cells, and more often of mucous membrane type.

The histological examination thus furnishes valuable indications, since the cancers of undifferentiated cells of mucous membrane type usually have a high radiosensitivity, while those of cutaneous type, highly differentiated, infiltrating and with epithelial pearls, have a minimal radiosensitivity. One can thus in a certain measure add to the histological as well as to the clinical examination, information which helps one to appreciate the type of cancer which one has to treat. It is always necessary to be prudent in this diagnosis when the cancers are very extensive. The peripheral parts of a neoplasm may seem mobile because they are papillary, while the lesions of the point of origin, which one begins to appreciate only fifteen to twenty days after the beginning of treatment, are often fixed and infiltrating. It is thus not always in the course of examinations preceding treatment that one can form an exact opinion as to the degree of immobilization. At times this is only possible in the course of daily examinations during treatment. Thus a histological examination made from the papillary portion of a neoplasm, of which the point of origin is an infiltrating type, can only give incomplete information as to the degree of curability.

One may classify topographically cancers of the larynx, from the standpoint of

roentgen therapy, into anterior, median and posterior sites.

The median cancers are in general more easily curable; they have a tendency to develop in a vertical direction, invading at times the band, ventricular cavity, cord, the parts adjacent to the cord, supraglottic, glottic and subglottic, but without extending anteriorly to the commissure, or posteriorly to the arytenoid. Moreover, they do not deeply infiltrate the cord, so that the whole of the larynx remains mobile, despite at times a considerable volume of tumor. These cancers remain median for a long time, but when they do gain the anterior and posterior parts of the larynx, they do so on the surface only; they seem incapable of infiltrating the dense connective tissues; they do not immobilize the muscles. Even though these epitheliomas be of cutaneous type, they are easily curable.

The anterior cancers often invade the epiglottic cartilage on its laryngeal surface; they readily traverse the cartilage and develop subcutaneously in the pre-epiglottic region. These are often curable, but less often than the median cancers. When this anterior type has invaded the anterior commissure, and has become fixed to the thyroid cartilage, or lower in the region of the cricoid cartilage, it is almost incurable, except when the histological form is undifferentiated.

The posterior cancers of the larynx rapidly invade the arytenoid and the posterior part of the cricoid ring, accompanied by a total fixation of the corresponding hemilarynx. They are rarely curable by irradiation.

These various classifications, according to the results of roentgen therapy, indicate to us that the histological form, the degree of mobilization or immobilization, the localization, the invasion of cartilage, must be the object of minute examination, because these are the indications which guide us in the choice of methods of treatment.

If we consider the two extreme cases, the cancer of mucous membrane type, of undifferentiated cells, and the cancer of cutaneous type of differentiated and infiltrating cells, the choice of treatment, of lesser importance in the first case, is essential in the second.

In the first case, a long treatment, continuous, by low daily doses of 275 r, for example, extending over thirty to forty days, for a total dose of 7,500 r, or even exceptionally 200 to 250 r daily for a total dose of 8,500 r in fifty days, has given us cures. This treatment is perfect in avoiding all local and general complications. But it is not as perfect in assuring a cure, particularly when some cells are slightly differentiated, because the daily doses, somewhat too low, are at the limit of the cancericidal effect. One can, however, treat this type of cancer by high daily doses, 500 to 600 r per day for several days, in a treatment of seventeen to twenty days' duration, and a total dose of about 6,000 to 7,000 r, as we did in 1921 and 1926 particularly. The risks of local accidents are greater, but the chances for cure are likewise greater.

In the second case, that of the differentiated type, it is absolutely indispensable to attain very high daily doses, because the threshhold of sensitivity is itself very high.

In intermediate cases, it is not necessary to attain such high daily doses—the threshhold of radiosensitivity being less elevated.

We shall further on give some information on the effects of irradiation in the two principal cases, and we shall show why the factor of the total dose is of interest in cancers of undifferentiated cells, while the factor of the daily dose is of little interest in these cases. We also shall show that, inversely, the factor of the daily dose has a greater importance than the total dose in the cancers of differentiated cells—that the more a cancer is differentiated, the more is it necessary to increase the daily doses rather than the total dose.

EFFECTS OF IRRADIATION ON CANCERS OF UNDIFFERENTIATED CELLS AND OF DIFFERENTIATED CELLS

In résumé, in the two extreme types of epithelioma of the larynx, the type formed

of undifferentiated cells of mucous membrane type, and that of very differentiated cells of cutaneous type, our results are inverse. They are very good for the former, they are very poor for the latter. The effect of our treatment on these two groups of cancers seems opposite. The one is very radiosensitive, easily curable, the other is little radiosensitive, rarely curable.

A short review of the effects of irradiation renders comprehensible this variance of results.

Irradiation produces diverse modifications: (1) in the normal and neoplastic epithelial cells, where the essential modification is the destruction of the cell; (2) in the vascular connective tissue, varying from a slight local congestion, transient, and repeated periodically, to a fibrosclerotic transformation of this tissue.

A. Cancer of Undifferentiated Cells. Summation of the Individual, Unicellular Epithelicidal Effects. In a cancer of the larynx formed of undifferentiated cells, the life of a cell is primitive; it is not intimately related to its milieu. All the daily doses, whatever their quantitative value, add together, accumulate, to produce a neoplastic epithelicidal effect. This neoplastic radioepithelitis, not absolutely confluent, is maintained each day without interruption by successive irradiations up to the total disappearance of the neoplasm, *on condition that the daily doses are distributed without interruption*, namely, daily. This is the continuous treatment. In other words, all the most variable of daily doses, from a minimum of 125 r, to a maximum of 1,000 r per day (this dose of 1,000 r can only be given consecutively for two to three days), are useful, *and the effects produced by the total dose are thereby the sum of the effects produced by each daily dose.*

There being no intimate union between the cells and the organism, no complex physiological phenomena, no modification of the vascular connective tissue interpose, between the irradiation and its effects on the undifferentiated neoplastic cells. If by chance a treatment really too intense greatly modifies a loose vascular connective tissue, in the midst of which are living undifferentiated cancer cells, no particular difficulty arises, because the neoplastic cells are in a large measure destroyed well *before* the appearance of modifications in the connective tissue.

The epithelicidal and connective tissue effects are successive, without any influence one upon the other. The epithelicidal effect is early, *it always appears before the thirteenth day*, at times after the fifth day, and the fibrosclerotic effect is late, not appearing before the thirtieth day.

This roentgen therapy is direct, quantitative, dosimetric, that is to say the effects are relatively proportional to the doses. These effects are simple, elementary, and in a certain measure the total dose can at times compensate for an insufficiency of some daily doses.

B. Cancers of Differentiated Cells. Antagonism of Effects Produced by Irradiation. In a cancer of the larynx formed of differentiated cells, the life of a cell is complex; it is subordinated to its milieu. After fifteen to twenty days of efficacious irradiation, that is to say, destruction of certain groups of cells which are notably the most radiosensitive, the effects suddenly cease, the cells show no further modification. One thus notes two phenomena which indicate failure and an aggravation of the local condition. There is a reduction in mobility of the neoplastic and surrounding general tissues. This is followed in three to four days by the appearance of a diffuse edema, particularly marked in the region of the arytenoid cartilage, an edema which rapidly increases. These are two guarantees of the inefficacy of the treatment. The daily doses have been incapable of destroying the most resistant cells. The daily doses were too low; or, high enough, they were not given at an opportune moment. They have moreover been disadvantageous, because they have modified the vascular connective tissue, and rendered difficult the nutrition of the neoplastic cells—thus they have reduced a radiosensitivity already too low.

When the neoplastic and general tissues have lost their mobility in this manner, each further irradiation accentuates the immobility, pain and edema, and impairs the general condition of the patient. When the moment favoring curability has passed, any continuation of irradiation, any increase in the total dose, render the incurability more absolute and only aggravate the accompanying symptoms.

Thus irradiation in these cancers is inefficacious because the cells have a fleeting, transient radiosensitivity, and also because the connective tissue has particular characteristics.

The more fibrous a vascular connective tissue is, having characteristics approaching those of tendon and muscle, the earlier is the fibrosclerotic effect. Moreover, the more a cancer is differentiated, the more rapidly does the peritumoral and intratumoral vascular connective tissue tend toward a fibrosclerotic transformation. But, as for the neoplastic cell, *the more a cancer is differentiated, the later the epithelicidal effects appear.*

If, then, a cancer of differentiated cells develops in the region of a tissue which is fibrous, tendinous, or mixed with muscular fibers, the fibrosclerotic effect always appears in the course of treatment. Frequently it is superimposed on the epithelicidal effect, and the sterilization of the neoplasm thus becomes impossible. Moreover, since one is obliged to give high daily doses to attain the threshhold of destruction for the differentiated neoplastic cells, one finds oneself led thus to accelerate, involuntarily, the appearance of the fibrosclerotic process.

It is the opposite case of that observed in epitheliomas of undifferentiated cells. In these latter, there is no reciprocal influence of the two effects produced by irradiation, while here we find a real antagonism between the fibrosclerotic and epithelicidal effects. *The total dose has lost its importance, since it is no longer the sum of the daily doses, but the difference between the useful and useless doses.*

Quantitative roentgen therapy is of little efficacy here because the effects produced are complex, indirect, antiphysiological. Roentgen therapy could and should become qualitative, and its effects would thus be physiological.

All these facts, easily controllable in the larynx, pharynx and buccal cavity, lead us to the conception of two general forms of roentgen therapy:

(1) Quantitative roentgen therapy, which is simple and elementary, in which the total dose and the continuous treatment are the principal factors.

(2) Qualitative roentgen therapy, which is physiological, and in which the high daily doses given at opportune moments, constitute, together with its discontinuity, the two principal factors.

Vol. 40, No. 4

RADIATION THERAPY OF CHRONIC MASTITIS*

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CHRONIC mastitis has for many years been a difficult problem for both pathologist and clinician. To the pathologist the fundamental basis of the process is still in some doubt, for in a single diseased breast there may be evidence of a functional disturbance, signs of inflammation, and beginnings of new growth. With even the nature of the disease undecided and the cause still a subject for theory, the clinician faces a difficult problem in his attempts at treatment.

In the early history of the therapy of this disease, the surgical approach predominates. There were many reasons for this, the most important being perhaps that no other agents were at first available. The disease, as then described, however, was a very active process. Surgical excision is probably still the best therapy for the condition described by Schimmelbusch, but this is not the lesion usually underlying the painful breast or simple discharging nipple which now brings so many patients to the clinics. Surgery is not justifiable in the mild diffuse forms of chronic mastitis, for here, if the diseased portions of the breast are all removed, the mutilation of the operation is out of proportion to the severity of the disease.

That many cases of breast disease are primarily the result of some disturbance in gland function and are not neoplasms is now widely accepted: The best evidence supporting such a view is the increase in symptoms before the menstrual periods and the marked improvement which usually occurs at the menopause. Proof of any specific endocrine disease underlying chronic mastitis has never been presented, and investigators have been forced to describe the theoretical ovarian dysfunction in the vaguest terms.

With the increased interest in the hormone factor in breast disease, which began a few years ago, it was a natural step to attempt a hormone therapy for chronic mastitis. Ovarian extract was at first given in the form of tablets of desiccated ovarian gland, and successes were at once reported. These improvements were evidently spontaneous remissions, for the substances first employed must now be regarded as having contained no significant quantity of hormone. The impetus given to glandular therapy by these apparent successes with desiccated ovarian extracts served, however, to launch the potent preparations of estrogenic substances when they became available. The rationale for estrogenic therapy is at best tenuous, and experience shows that there are many cases of chronic mastitis completely unaffected by this form of treatment. Therapy with the ovarian hormone will probably often continue to fail, because this substance has as its function the stimulation and not the suppression of breast growth.

With surgery contraindicated in the diffuse forms of chronic mastitis and with the estrogenic hormone often ineffective from a practical standpoint, and apparently contraindicated from a theoretical one, there remains a group of cases for which an adequate therapy must be sought. The present article is a report on a small series of such cases treated by irradiation with an attempt to evaluate the results.

From a clinical standpoint, cases of chronic mastitis present themselves in two principal forms:

(1) The cases in which pain is the predominant symptom. In the severe examples of this type, the breasts hypertrophy and a diffuse nodularity develops, especially in the outer quadrants. The patients

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

complain of a constant soreness, which increases before the menstrual periods and is accompanied by a sense of weight and pain which is often severe enough to cause loss of sleep. The histology of this form has not been finally determined, but in some cases at least a fibrosis of the lobular connective tissues is a prominent feature.

(2) The second type is characterized by secretion of some type from the nipple, serous, milky, or sometimes thick and pastelike. There is moderate pain in some cases, but this is not as constant or as severe as in the other type. The clinical signs are most marked in the central portions of the breast about and beneath the areola,where dilated ducts can often be individually palpated. Secondary inflammations are not uncommon. Microscopic examination of this type discloses a dilatation of the ducts, stasis of secretion, and a periductal infiltration of lymphocytes. Although mixed forms are not uncommon, the two diseases are perhaps distinct entities. Certainly many of their clinical characteristics are different and they respond differently to radiation therapy.

Radiation may be used in the treatment of chronic mastitis according to two distinctly different theories:

(1) Direct irradiation must produce definite tissue changes if it is to relieve symptoms. It may accomplish this by destroying epithelium, by reducing vascularity by its effect upon the vessel walls, by producing a fibrosis or possibly by acting upon sensory nerve endings. Any of these effects will require large doses, because the structures to be influenced are at least relatively resistant to radiation.

(2) The second method of radiation therapy of chronic mastitis is an indirect one, by which an atrophy of the breast is produced through artificial suppression of the ovarian function. The amount of radiation required is small because of the extreme radiosensitivity of the granulosa cells of the ovarian follicles.

(1) *Direct Irradiation of Cases of Chronic Mastitis.* Detailed reports on the effect of roentgen irradiation on chronic mastitis are almost absent in medical literature. Frequent passing references suggest, however, that many physicians have attempted radiation treatment in occasional cases (Dietrich and Frangenheim, Meyer, Cutler, Keynes, Kozhevnikoff). Webster, in 1928, referred briefly to the satisfactory results obtained in 90 per cent of his 60 cases treated with four "medium or high voltage treatments cross-firing the breast." Knoflach and Urban have described 4 cases of bleeding nipple with cessation of the discharge after two to four roentgen treatments, but they recommend this form of therapy only when operation is contraindicated or refused. Reynolds more recently has reported success in 150 cases which, depending upon the type of mastitis, he treated with voltages of 80 to 180 kv., giving as a rule three treatments of one-half an erythema each at weekly intervals.

Selected cases of chronic mastitis have been treated by direct roentgen irradiation for several years at the Memorial Hospital. It has remained a method to be used only in patients with severe or persistent symptoms. The present report of 22 cases includes several from the earlier years of low voltage therapy, some from a period during which the dosage with high voltage roentgen rays was gradually being increased, and a few recent cases systematically handled by a divided dose technique.

Of the 22 cases treated by direct roentgen irradiation, 18 were married, and all of these had had children. The ages of the patients varied from twenty-seven to sixty-six, the average being forty years. The average duration of symptoms was two years. Of this group, 17 suffered from pain of at least moderate severity, and 11 had secretion from the breast of some type. Following treatment the patients have been observed for periods of time, ranging up to six years and averaging two years. In general, the cases were of rather more than the average severity and, in most, other methods of treatment had failed before roentgen therapy was resorted to.

Table 1 shows the variable results obtained when chronic mastitis is treated by direct roentgen irradiation of the breast. The difficulty of evaluating degrees of pain and amounts of secretion, as well as the extent of nodularity, must be remembered in interpreting the table. The final column entitled "effect on the patient" is made up from a general consideration of all the notes in the chart following therapy, often covering several years of visits at intervals of a few months.

TABLE I

RESULTS OF TREATMENT BY DIRECT IRRADIATION OF THE BREAST

	Effect on Pain 17 cases		Effect on Secretion 11 cases		Effect on Nodularity 22 cases		Effect on Patient
Time after treatment	6 mo.	Later	6 mo.	Later	6 mo.	Later	
Cured	4	7	1	3	5	11	5*
Improved	7	1	6	5	9	1	9
No change	6	6	4	2	8	6	8

* Two cases of this group had an almost simultaneous natural menopause.

Review of the types of therapy given shows the wide variety of methods used. Among the 5 patients "*cured*" only 1 received low voltage therapy, and this patient simultaneously experienced a spontaneous menopause which probably contributed to the improvement. Two received single high voltage (200 kv.) treatments and of these 1 also soon after noted a cessation of menstruation. Finally, 2 patients received a total of 1,200 r, given in three treatments. Among the patients "*improved*," 4 received single high voltage treatments, amounting to 600 to 750 r, and 5, divided dose treatments amounting to 1,200 to 1,800 r. In 2 of the latter the cycles of divided dosage were repeated. Of the 8 "*failures*" 2 received low voltage; 1, low voltage to one side and high voltage to the other; 3, single high voltage treatments; and 2, divided dose therapy. The first of the latter received 1,200 r in three treatments; the second 600 r in two treatments and six months later 1,000 r more in two treatments.

From this analysis it appears that in severe cases of chronic mastitis, relief from pain cannot be counted upon, and complete relief is exceptional even when relatively large doses of roentgen rays are given. Nevertheless, in well over half of the cases some relief of pain was experienced, and this seemed somewhat more likely to occur with the larger dosage and with high voltage than with smaller dosage or with low voltage. Relief from secretion also follows some of these treatments. That better results might be obtained by still larger doses is possible, but it must be remembered that the skin changes following very heavy irradiation may themselves be associated with uncomfortable sensations easily exaggerated by the nervous patient with breast disease.

The frequency of improvement in these cases may be said to be no greater than is to be expected from the well-recognized spontaneous remissions of the disease. This objection might be valid were these not selected cases of known persistence and resistance to other methods of therapy. That large doses of roentgen rays do have a definite effect on non-malignant diseases of the breast can best be shown by the unilateral improvement in symptoms and reduction in size when one breast is treated and the other kept untreated as a control.

R. F., admitted on May 15, 1934, was a married woman, aged forty, with 3 children, the youngest twelve years old. Her present illness consisted of a constant bilateral breast pain of three weeks' duration. Examination showed the breasts to be of medium size, pendulous in shape and with areas of mastitis in

both outer quadrants. The right breast was more affected and contained a relatively circumscribed area of mastitis, 7×5×2 cm. in diameter.

The patient was observed in the clinic for three months, during which time she received injections of an estrogenic hormone with some temporary improvement, but the symptoms soon returned.

From August 12 to August 15 the patient received on alternate days three roentgen treatments to the right breast, totaling 1,200 r, the factors being 198 kv.; 0.5 mm. Cu; 50 cm. target skin distance; 30 ma.; time, seven minutes; with 10.3×10.3 cm. fields. Four months later the right breast was softer than the left, and gave no symptoms. Eleven months after treatment, pain was still present in the breast not irradiated, but the right breast, formerly the larger of the two, was now the smaller and was free from the nodularity and evidences of hyperemia notable in the left one (Fig. 1).

Fig. 1. Reduction in size of right breast following roentgen treatment to that side.

From August 24 to August 27, 1935, the treatment previously given to the right breast was given to the left one. Five months later the patient was noted as symptom-free and the breasts soft. Eight months after treatment there was a little discomfort only in the left breast, but much less than before treatment.

(2) *Treatment of Chronic Mastitis by Irradiation of the Ovaries.* That improvement could be brought about in chronic mastitis by producing an artificial menopause was almost a certainty before the first case was attempted. It was known in the first place that chronic mastitis improved after the natural menopause. Furthermore the pain in most cases is usually moderate except before the menstrual periods, and without the periods the patient could expect at least to be spared the premenstrual exacerbation of pain and swelling.

The cases treated by irradiation of the pelvis are still only 18 in number, because the indications for this radical method of therapy are necessarily quite limited. The group included 2 unmarried women, 6 married but without children, and 10 who had had full-term pregnancies. The average age of the group was forty-one years, the youngest patient being thirty-three and the oldest fifty-one. The average duration of symptoms was ten months. Fifteen patients suffered from pain and 6 from some type of secretion from the nipple. Abnormal nodularity was present in all but 1 of the cases and quite marked in 5. The period of observation after treatment has varied from one to seven years, the average being four years. Here again the cases were of more than the average degree of severity, because the simple cases were never subjected to this form of therapy.

Table 11 demonstrates the almost complete dependability of the method for the alleviation of pain. When adequate roentgen irradiation to the pelvis is given to suppress the ovarian function, diminution in the swelling and tenderness of the breast begins within a few weeks, sometimes within a few days of treatment. Secretion, however, is not so easily disposed of, and often months after the disappearance of the symptoms of pain and swelling a drop of serous or milky secretion can be expressed from the terminal ducts.

In several cases the roentgen dosage was calculated to give only a temporary suppression of the ovarian function. In one group that had previously had a hysterectomy with preservation of the ovaries, it was possible to observe the coincident disappear-

ance of the breast symptoms and the development of the subjective sensations of the menopause and later a partial return of the breast symptoms, as the hot flushes disappeared. In 2 younger women, who were still menstruating, when treated by temporary roentgen castration, there was a return of breast discomfort with the reappearance of the menses. After such intervals of absent ovarian function and temporary breast atrophy, the symptoms when they returned were always less severe than before the interval of rest.

Beginning on April 4, 1933, the patient's urinary excretion of estrogenic hormone during the course of a menstrual cycle was measured by the Frank method and found to be 2,300 mouse units. The blood contained a mouse unit of estrin in 40 cc. of blood in the first and third week. The determinations for urinary prolan were negative (Fig. 2).

On account of the persistence of the patient's symptoms, and with her evident sterility as further justification, temporary roentgen castration was decided upon. Beginning on June 5, 1933, she received four roentgen treatments of 200 r each to the pelvis on four successive days, the factors being: 198 kv.; 0.5 mm. Cu; 50 cm. target skin distance; 15.6×13.0 cm. fields; 30 ma. for three minutes.

TABLE II

RESULTS OF TREATMENT BY IRRADIATION OF OVARIES

	Effect on Pain 17 cases		Effect on Secretion 11 cases		Effect on Nodularity		Effect on Patient
Time after treatment	6 mo.	Later	6 mo.	Later	6 mo.	Later	
Cured	8	8	1	3	6	12	9
Improved	7*	7	2	0	9	5	8*
No change	0	0	3	3	2	0	1†

* Five of these were free of symptoms during temporary suppression of ovarian function.
† Patient showing no change had no symptoms except secretion.

That the breast symptoms are closely related to the ovarian hormone can be demonstrated by studying the quantities of estrogenic substance excreted in the urine before, during and after this roentgen therapy. The following cases are illustrative:

R.K., a woman aged thirty-three, married for nine years but sterile, was admitted on October 1, 1931. Four years before admission she had undergone an operation for removal of a uterine fibroid and a small cyst of the right ovary. Since this operation her menstruation, formerly lasting four days, had been reduced to one, although remaining quite regular.

For two years there had been tenderness and enlargement of the breasts, especially the right one, with a definite seven-day premenstrual exacerbation of the symptoms of pain and swelling. Examination showed the breasts large and pendulous, with diffuse areas of thickening in both outer quadrants, especially the right one. The pelvic examination showed a small, retroverted uterus, but no other abnormality.

The patient was kept under observation for two years, during which time the symptoms persisted despite estrogenic hormone therapy by mouth and by injection.

The patient had menstruated on June 6 and it was accordingly hoped that she would not menstruate again. This hope was not realized, however, because a regular period, preceded by the typical breast symptoms, began on July 4. The hormone studies, however, were in harmony with these symptoms, for from June 6 to July 4, the excretion amounted to 2,834 mouse units and prolan was still absent (Fig. 2).

Following this period, however, the breast symptoms rapidly subsided and the menstruation did not occur on the expected date. Beginning August 29, with the breasts symptomless and the artificial amenorrhea apparently established, a further month's analysis was undertaken. Only traces of estrin were detectable amounting to perhaps 50 mouse units for the entire month, but prolan was still absent. The patient remained under observation for a year without return of breast symptoms or menstruation.

Another case illustrates the persistence of improvement even after the return of ovarian function.

E.B., admitted September 9, 1929, was a colored woman, aged thirty-seven, divorced, with a single pregnancy ending in a miscarriage sixteen years previously. Three years before admission she had had a supravaginal hysterectomy and unilateral oophorectomy for myoma and cystic ovary. Some milky secretion had been present in her breasts since her miscarriage, but two years after her operation there had been a sudden development of swelling and tenderness of the right breast. More recently the left had been similarly affected.

Examination showed the breasts to be of medium size, erect, with the right breast considerably larger than the left. Both were exquisitely tender with circumscribed areas of induration in both outer quadrants. Large quantities of what appeared to be true milk could be expressed from both nipples. Pelvic examination showed the absence of the uterus and the presence of a small mass above the right fornix, apparently a cystic ovary.

A few days after admission the patient received high voltage roentgen therapy to the right pelvis, the factors being: 175 kv.; 0.5 mm. Cu; 50 cm. distance; 60×60 cm. fields; 30 ma.; time, twelve minutes. This corresponded to a dose of approximately 600 r to the skin. Within four weeks the pain had practically disappeared, and after two months the breasts were soft and nearly equal in size. The secretion from the nipple had continued, and hot flushes had developed.

At the end of eleven months the hot flushes began to disappear, and there was a partial return of breast discomfort. During the next three years there was slight pain at times, but nothing in any way comparable to the condition preceding the roentgen therapy. The secretion gradually diminished.

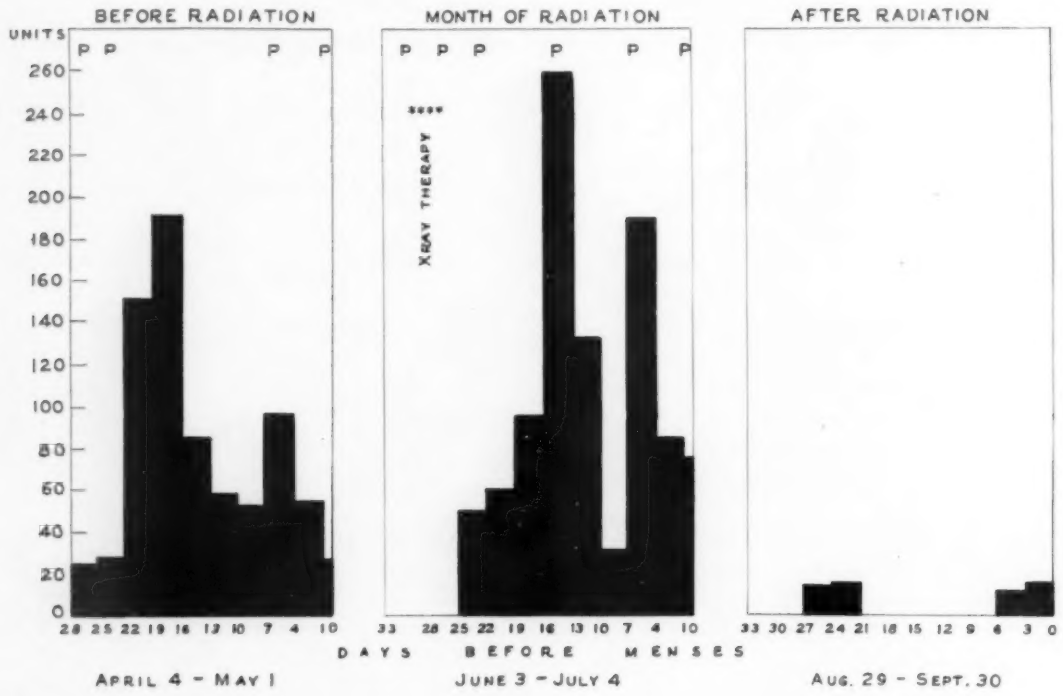

Fig. 2. Excretion of estrogenic substance before, during and after irradiation of the ovaries. (P = pain.)

Analysis of the estrogenic hormone excretion, begun on February 6, 1933, showed the average of four twenty-four-hour specimens obtained at weekly intervals, to be 152 mouse units, while the average of nine similar specimens, begun October 2, 1935, was 175 mouse units. Prolan was not found in increased amounts in the urine. This patient undoubtedly had a return of an active ovarian function, but without the reappearance of her severe breast symptoms.

The study of even this small series of cases shows that as a rule complete elimina-

tion of the symptoms of pain and swelling can be expected when the ovaries are irradiated. The abnormal nodularity of the breast will usually be reduced. Secretion from the nipple, however, frequently persists for some time, possibly for several years, and is evidently not so directly affected by the loss of ovarian secretion. Smaller doses, to give a temporary suppression of the ovarian function, are likewise accompanied by improvement. When the ovarian function re-establishes itself, some return of the breast symptoms is to be expected, but these are usually not so severe as before the interval of ovarian rest.

DISCUSSION OF INDICATIONS

The majority of cases of chronic mastitis fall into categories which must be excluded from radiation therapy: (1) First of all, circumscribed masses require surgical excision. This is essential if disastrous mistakes in diagnosis are to be avoided. (2) Mild cases of mastitis should receive no active treatment. Support of the breast, encouragement and reassurance, elimination of fatigue and worry will usually serve to reduce the symptoms markedly. Irradiation of the breast or ovaries is meddlesome interference in such patients.

There remains a small group of cases with diffuse breast disease and symptoms so severe as to demand relief. If the patient is over forty, if she has had a sterilizing pelvic operation, or if for evident reasons there is no probability of the patient's desiring children, roentgen castration may be undertaken with the practical certainty that symptoms will be improved. If the patient desires it, a smaller dose to cause temporary sterilization only may be given. This will produce temporary relief and probably permanent improvement, and the larger dose can be given later if desired.

If the patient is younger and desirous of retaining her fertility and menstrual function, direct roentgen irradiation of the breast may be undertaken. Relatively large doses of high voltage roentgen rays are essential if any results are to be obtained. The patient should be warned that improvement probably will not be complete and that some skin pigmentation is to be expected. In spite of these drawbacks, there are certain severe cases in women in their twenties and thirties in which such therapy is the best that can be offered. Direct roentgen irradiation of the breast is a less radical therapy than any type of irradiation to the pelvis.

SUMMARY

Twenty-two cases of chronic mastitis treated by direct irradiation of the breast are reported with improvement noted in about two-thirds. Eighteen cases of treatment of chronic mastitis by irradiation of the ovaries are reported with improvement in seventeen. The indications and contraindications for these methods are discussed.

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OSTEORADIONECROSIS IN INTRAORAL CANCER*

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THE improved results which have followed the use of roentgen rays and radium in the treatment of intraoral cancer have justified their widespread employment as therapeutic agents. Neoplasms having their origin in the tissues about the head and neck are particularly well suited to irradiation measures.

Surgical treatment alone does not give satisfactory end-results in this group of cases because of failure to control the soft part extensions of the disease. But, on the other hand, it has been found that irradiation alone, although adequate for the control of the disease in the soft tissues, may fail to eradicate cancer when it has invaded any of the surrounding bony structures or when infection and cancer together are present in the bone.

Intraoral cancer could undoubtedly be eradicated more promptly and satisfactorily by the radiation facilities now at our command if it were possible to raise the dosage in each case to the necessary level and still not produce necrosis of the surrounding normal structures, especially bony tissue. It has been recognized that the responsibility for the serious complication of osteoradionecrosis rests entirely with the physician who outlines and carries out the irradiation measures, just as the surgeon must assume the major responsibility for an operative death.

Osteoradionecrosis is a frequent complication. It is so striking and often so rapid and explosive in its onset and so serious in its resultant morbidity and mortality that it appeared worth while to review the recent literature on this subject, together with a large consecutive group of cases from the Head and Neck Service at the Memorial Hospital, in the hope of shedding some light on the etiology, course and prevention of this unhappy and frequent sequel to the treatment of intraoral cancer. At Memorial Hospital most cases of intraoral cancer receive either radiation therapy alone or in conjunction with surgery.

HISTORY OF THE ACTION OF RADIATION ON BONY TISSUE

Soon after the discovery of roentgen rays experiments were carried out to determine their effect on living tissue. In 1903 Perthes reported the first observations on the effect of roentgen rays on living and growing bone. He exposed the right wing of one-day-old chickens to roentgen rays and at the end of twelve days found that the growth of the treated wing had been considerably stunted, and its feathers were thin and small. This original observation has been frequently rediscovered.

Recamier in 1905 was able to demonstrate the inhibitory effect of roentgen rays on the growth of bone. He later observed that growth of bone could be inhibited by a dose of roentgen rays so small as to produce no skin effect and no histological evidence of cellular change in the bone. It remained for Cluzet in 1909 to demonstrate delay in the callous formation which resulted when fracture sites were exposed to roentgen radiation. He also observed that this delay could be caused by radiation given either before or immediately after the fracture was produced. He was also first to note the definite histological changes which occurred in the irradiated fractures. Wilkins and Regen found that moderate doses of roentgen rays given previous to the production of a fracture in adult rabbit bone resulted in marked delay in union and in inhibition of the rise in phosphatase activ-

* From the Head and Neck Department, Memorial Hospital, Service of Dr. Hayes E. Martin. Presented at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

ity that normally accompanies the healing of a fracture. They discovered further that the phosphatase activity of growing dog bone was markedly reduced following moderate doses of roentgen rays.

In experiments to determine the results of repeated exposure to doses of roentgen rays sufficient to inhibit bone growth, Brooks and Hillstrom showed that a given total quantity of radiation received always produced less inhibition of bone growth the larger the number of times that dose was divided or the longer the interval between the exposures; that is, 150 per cent of a skin erythema dose given in two equal doses on successive days had the same bone growth inhibiting effect as a single dose of 100 per cent of a skin erythema dose, and 160 per cent of a skin erythema dose given in four exposures over a six day period produced less effect than a single 100 per cent skin erythema dose.

Some facts as to the actual cellular effect of roentgen therapy on adult bone tissue are known, but no reports on the effect on bone of roentgen therapy given by the fractionated dosage principle are as yet available. The measurement of the secondary radiation given off by bone also needs investigation. Clinically, however, it is certain that heavy external irradiation produces changes in bone which diminish its powers of resistance to infection and increase its susceptibility to infection and trauma. Stevens reports the occurrence of staphylococcus osteomyelitis in the femur of a child which had been heavily irradiated four years and nine months previously. Dalby, Jacox and Miller, in this country, have reported 14 cases of fracture of the femoral neck following pelvic irradiation for gynecologic cancer and suggest that the irradiation may have been an important factor in producing this complication. Three similar reports appear in the European literature (Baensch, Kropp and Philipp). Spontaneous fracture occurring in irradiated rabbit legs has been noted by Whiteleather in his experiments.

To understand the reaction of bone to irradiation one must recall the definite and peculiar gross and histological architecture of this tissue. Bone cells are derived from osteoblasts which have become enclosed in a bone space or lacuna. These bone cells are connected one with the other and receive nourishment through very fine processes known as canaliculi. The outer surface of the bone receives a large portion of its nourishment from the periosteal blood vessels which enter its substance through Volkmann's canals. The blood vessels of the haversian canals and the nutrient artery supply the deeper portions of the bone and the marrow. This blood system forms a rich vascular network enclosed in a rigid framework of bone tissue, the structure of which makes it highly vulnerable to the effect of irradiation.

HISTOLOGICAL CHANGES IN BONE PRODUCED BY IRRADIATION

Ewing states that different tissue reactions are excited by the three main methods of radiation treatment: the single massive dose, the fractionated dose and the prolonged continuous dose. For an understanding of adult bone reaction to the last two methods of treatment further investigation is necessary, but histological evidence is available regarding osseous tissue treated by variations of the first method.

The periosteum is highly susceptible to irradiation. After sizable therapeutic doses, gross swelling and thickening occur and the periosteum strips easily from the bone. On histological examination the inner surface of periosteum presents a thick hyaline layer without cells. The layer of osteoblasts usually found on the inner surface of the periosteum in contact with the bone may be absent. This undoubtedly explains the lack of bone regeneration after sequestrectomy or subperiosteal jaw resection. The arterioles may be strangulated by a post-irradiation swelling of all the coats comprising the walls of these vessels. The effect of irradiation on the lymphatics of the periosteum is not clearly understood.

The bone itself following irradiation of-

ten shows osteoporosis, the trabeculae are narrowed and irregular and the volume of fatty marrow is increased. The bony structure is less substantial and extensive obliterative sclerosis of the nutrient vessels takes place. The bone cells show degeneration and stain poorly with hematoxylin and eosin. The lamellar bone appears hyaline and very brittle, canaliculi are closed, and the capillary circulation is imperfect.

Table I

OCCURRENCE RATE FOR OSTEORADIONECROSIS IN RELATION TO THE LOCATION OF THE PRIMARY INTRAORAL CANCER. THE ALVEOLAR RIDGE IS THE MOST COMMON SITE AND THE LIP CANCERS TREATED BY IRRADIATION SELDOM DEVELOP BONE COMPLICATIONS

Location of Primary Lesion	No. of Cases Treated	No. of Cases Developing Osteoradionecrosis	Percentage
Alveolar ridge	121	48	40
Floor of mouth	180	62	34
Buccal mucosa	149	37	25
Tongue	541	55	12
Tonsil	206	11	5
Lip	622	22	3.5
Total	1819	235	13

Regaud states that the lamellar portion of bone is the most susceptible to roentgen radiation, but Nageotte thinks the bone cells are more susceptible than the bone lamellae and much more likely to be killed by the radiation. Ewing suspects that the cells are killed first and then late changes occur in the lamellar substance leading to devitalization.

Calcium phosphate with an atomic weight of 40 makes up 85 per cent of the mineral content of bone. When bony tissue is irradiated, this high calcium content is partly responsible for transforming the hard, penetrating, primary radiation to a less penetrating, more absorbent, more caustic and selective type of secondary radiation. From this it is apparent that the periosteum, and especially the inner layer of osteoblasts of the periosteum, receive both primary radiation and the maximum effect of the caustic secondary rays. As Regaud says, "The irradiated bone burns and burns the periosteum and mucosa enveloping it."

CLINICAL MATERIAL

In order to obtain a comprehensive view of the clinical problems presented by osteoradionecrosis, it was thought advisable to examine the material of the Head and Neck Service at Memorial Hospital during the seven-year period between January, 1930, and January, 1937. During this seven-year interval 1,819 patients with intraoral cancer or allied conditions were accepted for treatment (Table I). The statistical portion of this report is based on a review of this group of case histories. Certain inaccuracies are unavoidable. A small number of the patients did not accept treatment, some were in poor condition on admission and were unable to complete the treatment outlined, a few were lost to follow-up. Nevertheless, the total of 1,819 cases is used in figuring percentages.

Of the group studied there were 235 patients in whom osteoradionecrosis was demonstrated either clinically or roentgenographically, that is 12.9 per cent, or 1 patient in every 8 had on admission or later developed the complication of osteoradionecrosis. Even though this figure seems high, it might be well to point out that we know from experience that late osteoradionecrosis is likely to occur even eight and one-half years after successful treatment (Fig. 1). Therefore a certain number of cases treated during 1936, and included in this series, will probably develop bone involvement eventually. The true percentage will consequently be even higher.

As is usual in intraoral cancer, there were more male than female patients, 215 men (91.5 per cent) and only 20 women (8.5 per cent). The complication of osteomyelitis occurred at a later age in men where the average was fifty-seven years than in women where the average was forty-eight years (Table II). The youngest male was thirty-three years old and the oldest was seventy-

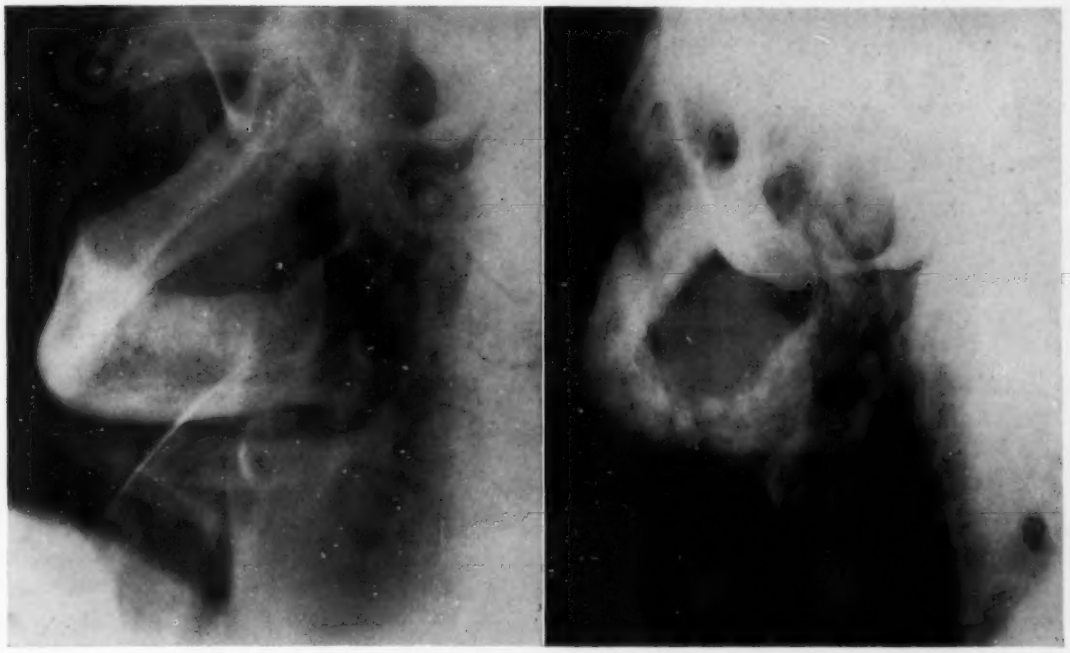

Fig. 1. Osteomyelitis developing in an irradiated mandible three years after roentgen treatment.

nine. The youngest female was twenty-five and the oldest was sixty-seven.

The primary tumor was located in the floor of the mouth in 62 cases, in the tongue in 55 cases, on the lower alveolar ridge and mandible in 48 cases, on the buccal mucosa in 37 cases, on the lip in 22 cases and in the tonsil in 11 cases. In comparing the number of patients developing bone complications in each location with the total number of patients treated in each of these groups, we note that 40 per cent of the alveolar ridge cases developed osteonecrosis, but in only 3.5 per cent of the lip cases did bone tissue become involved.

The reasons for the development of osteoradionecrosis are fairly obvious. The patients are usually well past middle age, at a stage in their lives when a certain amount of osteoporosis is fairly common, and the early stages of arteriosclerosis of the vascular structures of bone are to be expected. Even before treatment is started, the intraoral condition is often deplorable due to neglect of the ordinary oral hygienic measures. Of 170 patients in whom satisfactory data regarding teeth were obtained, there were only 7 instances in which the teeth were in good condition; 100 had poor teeth, 27 had fair teeth and 36 were edentulous. Such patients are not apt to care well for their mouths during a painful irradiation reaction. Irradiation produces a stomatitis, further reduces the blood supply to periosteum and bone, decreases bone cell activity and resistance to infection. With a poor dental condition already present the stage is set for pathogenic organisms to find their way between the loosened teeth and the gum margins down to bone and set up an acute suppuration.

Table II

Age and Sex Distribution of 235 Cases of Osteoradionecrosis

	Males	Females
No. of patients	215	20
Average age	57.5 years	48.1 years
Youngest	33 years	25 years
Oldest	79 years	67 years

The extraction of teeth after heavy intraoral irradiation is a hazardous procedure. In 94 patients extractions were carried out;

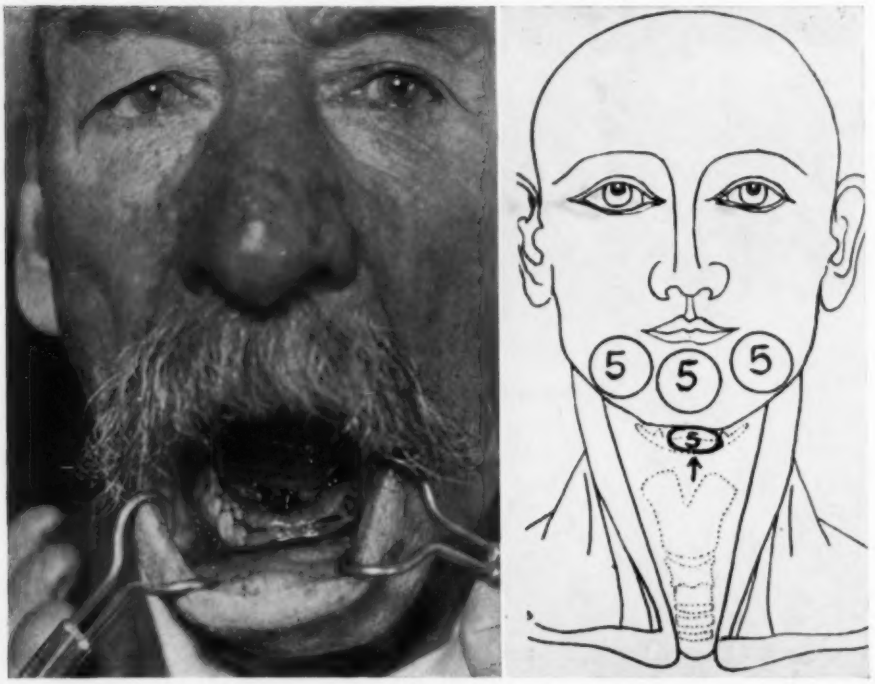

Fig. 2. Extensive osteomyelitis and loss of bone substance as a late result of heavy roentgen irradiation through the mandible for cancer of the anterior floor of the mouth. *Treatment.* Roentgen therapy December 26, 1934, to February 15, 1935: 200 kv., 30 ma., 0.5 mm. Cu filter, 63 cm. target-skin distance, 200 r every two days, four portals 5 cm. in diameter; left and right jaw, submental and anterior chin—total 4,000 r×4. Radium therapy March 8, 1935: three gold tubes for a total of 7.5 mc. anterior floor of mouth.

38 before irradiation measures were instituted and 56 afterward. In 9 patients several teeth were extracted after osteomyelitis was present. In reviewing this group of cases it seems to us that, although osteoradionecrosis may occur whether teeth are

removed before or after irradiation, it is more logical to remove all condemned teeth before irradiation. Otherwise such teeth present a continuous peril to the patient cured of his cancer, for we know that during the ensuing years these teeth with their diminished blood supply are likely to develop cavities, become soft, crumble or loosen, and on extraction permit introduction of infection into the devitalized maxilla. This sequence of events may occur even as late as four years after the patient has been treated and cured of cancer. Other mechanical or chemical traumas such as the application of iodine to a healed intraoral radiation scar have caused the onset of a fatal osteoradionecrosis of the mandible.

From this it will be seen that three definite etiological factors are involved in the production of osteoradionecrosis: first, irradiation, then trauma, followed by infection (Fig. 2).

In a small percentage of patients the clinical course of events would lead one to surmise that the irradiation had sterilized and healed the soft part cancer, but that a few malignant cells, having permeated the periosteum and invaded bone, had been incompletely eradicated. After several months of freedom from visible evidence of disease, during which roentgenograms of the bone have been negative, an abrupt onset of deep-seated activity occurs. The overlying scar ulcerates, infection occurs, and a severe and explosive type of bone necrosis takes place.

Syphilis is definitely not a factor in the etiology of these bone complications, but when a patient who has a four plus Wassermann reaction develops osteonecrosis his prognosis is less favorable than is the outlook for the average case. Wassermann tests were carried out in 159 cases and 141 gave a negative reaction and only 18 were positive. Of the 18 patients with positive Wassermann reactions, complete data are available on 17 and of these 10 died and of the other 7, one is alive with disease and osteoradionecrosis and is not expected to recover.

DIAGNOSIS

The early diagnosis of bone necrosis must be made on the symptomatology and on careful inspection, palpation and repeated observation. Roentgenograms are not of great diagnostic value early in the course of this disease. The roentgenographic difficulties here are similar to those encountered in the diagnosis of acute, early, suppurative osteomyelitis in children. Continuous, prolonged, dull, unrelieved pain limited to an irradiated mandible and described by the patient as similar to but worse than a toothache may precede by several months the actual onset of ulceration and suppuration. During this period the roentgen examination will be negative, but a suggestive thickening of the bone and periosteum may be detected.

When trismus, ulceration, soft part swelling, draining sinuses and exposed areas of bone are present, the process is of long standing and is easily diagnosed. At this stage the roentgenograms are positive. At a still later stage, pathological fractures oc-

TABLE III

125 CASES ARE DEAD AND IN 106 INSTANCES (85%) BONE COMPLICATIONS WERE A FACTOR IN THE CAUSE OF DEATH; 12 CASES (9.6%) DIED FREE OF CANCER AND AS A DIRECT RESULT OF OSTEORADIONECROSIS

Cause of Death	No. of Cases	Percentage
Osteoradionecrosis and cancer	67	53.6
Osteoradionecrosis; no cancer	12	9.6
Cancer; no osteoradionecrosis	5	4.0
Hemorrhage, cancer and osteoradionecrosis	14	11.2
Hemorrhage and osteoradionecrosis; no cancer	4	3.2
Hemorrhage; no cancer or osteoradionecrosis	2	1.6
Osteoradionecrosis, cancer and complications	9	7.2
Other causes	12	9.6
Total	125	53.0
Active 1-1-37 without disease	79	33.6
Active 1-1-37 with disease	16	6.8
Lost to follow-up	15	6.4
Total	235	

cur, sequestra form, and the diagnosis is obvious at a glance.

MORTALITY

Often the most advanced intraoral cancers are found in debilitated patients with the most unsanitary mouths. Such patients present a setting favorable to the onset of bony complications, while, at the same time, the body as a whole is least able to combat the combination of cancer, osteomyelitis and irradiation. One would naturally expect a high mortality rate. Of the 235 patients in this series, 125 are dead (Table III). Of the patients who died, 67 presented evidence of cancer and osteoradionecrosis at the time of death, while 12 patients free of cancer died directly as a result of osteonecrosis. Hemorrhage caused 20 deaths and there were 10 deaths from other causes in which neither osteomyelitis nor cancer played an important rôle.

MORBIDITY

Irradiated osseous tissue not only tends to lose its natural resistance to infection, but after suppuration occurs, the factors in the repair process are markedly depressed and sequestration is slow and painful. Indolent sinuses drain for months and years until the necrotic underlying bone is extruded. Pathological fractures of the mandible frequently occur and further incapacitate the patient. If a segment of the horizontal ramus of mandible is involved and sequestrates, a permanent loss of tissue results and the function of the part is reduced because the periosteum does not, in the average case, retain enough viable osteoblasts to permit bone regeneration.

Since elective treatment of osteoradionecrosis of the mandible is usually conservative in nature, and since the course of sequestrum formation is delayed and the repair processes slowed, a rather long average period of incapacity due to this complication is to be expected. In the present series 204 cases are suitable for morbidity statistics and the average period of incapacity for all cases treated conservatively is 11.1 months. The longest interval of continuous osteomyelitis was eight years and seven months and the shortest was one month.

TREATMENT

When intraoral osteonecrosis is once established, it is well to treat it conservatively (Table IV). General supportive measures should be employed to increase general resistance, and strict attention paid to diet with a daily supervision of the quantity and quality of the food intake. Due to trismus, painful swallowing, edema or salivary fistulae it may be necessary to provide sufficient food intake by means of the nasal feeding catheter. Daily adequate bowel elimination is essential as fecal impactions and constipation are apt to occur on a high caloric, liquid diet. Weekly blood counts may indicate a secondary anemia and the advisability of a whole blood transfusion.

TABLE IV

COMPARING THE CONSERVATIVE AND RADICAL METHODS OF TREATMENT FOR OSTEORADIONECROSIS. IN 31 CASES THE RECORDS WERE NOT SATISFACTORY FOR STATISTICAL PURPOSES

	Conservative (Sequestrectomy)	Operative (Jaw Resection)
No. of cases	164	40
Died	82	18
Recovered	63	18
Finalled	10	—
Active with osteoradionecrosis	9	4
Duration of osteoradionecrosis	11.1 months	9.3 months

Local measures are best carried out by the patient with frequent mouth irrigations of copious amounts of a warm sodium bicarbonate solution. An additional daily irrigation with a power spray and suction is advisable. Soft part abscesses should be opened and drained as they occur and sequestra removed when they become loose. Mild pain may be controlled by aspirin, or codeine with aspirin, but morphine is contraindicated because of the protracted

Fig. 3. Peroral roentgen irradiation for cancer of the anterior floor of mouth. The beam of roentgen rays is so directed as to spare the mandible as much as possible. The danger of late osteoradionecrosis is reduced.

course of the disease. Severe pain often necessitates an alcohol injection of the involved sensory nerves. In the case of mandibular pain the third division of the fifth cranial nerve is injected with 8 minims of absolute alcohol and instantaneous relief obtained.

Sequestrectomy under novocaine block anesthesia is often indicated and is frequently followed by prompt healing and cessation of pain. Resection of the inferior maxilla, if attempted late in the course of the disease, is a serious procedure carrying with it a mortality of 21.6 per cent in a series of 51 cases so treated.

PROPHYLAXIS

(*a*) Devitalized, loose, carious teeth should be removed before treatment is started, and, from our studies, the impression is obtained that recession at the gum margins and pyorrhea are indications for the pre-irradiation removal of such teeth if they are to be in the beam of radiation. When the operator contemplates utilizing a very heavy dose of external irradiation together with peroral irradiation, and possibly local interstitial radon, it is well to remove all such teeth. In certain instances even the sound ones in the immediate vicinity of the neoplasm should be removed for, after a period, these teeth may disintegrate due to a lack of adequate blood supply leading to eventual suppuration in the adjacent bone.

(*b*) When interstitial radium is used in the oral cavity, all possible protection of the uninvolved soft tissues should be obtained by protective dental molds containing the maximum amount of lead. These should be worn by the patient continuously, except during meals, for the entire irradiation period when removable implants are used, and for at least seven days when gold radon seeds are employed.

(*c*) External irradiation should be outlined and carried out, first of all with the idea of sterilizing the intraoral cancer. Next in importance, portals should be selected and the beam of radiation directed in such a fashion as to cause as little bone damage as possible (Fig. 3). Wherever feasible, small, round portals should be used and the size reduced as the tumor regression takes place. The uninvolved soft parts and bone should be protected by the use of peroral portals and suitable lead shields.

(*d*) As 40 per cent of the patients with cancer of the lower alveolar ridge and 34 per cent of those with cancer of the floor of the mouth develop serious bone complications, it is wise to attempt to determine, before therapy is outlined, just which cases

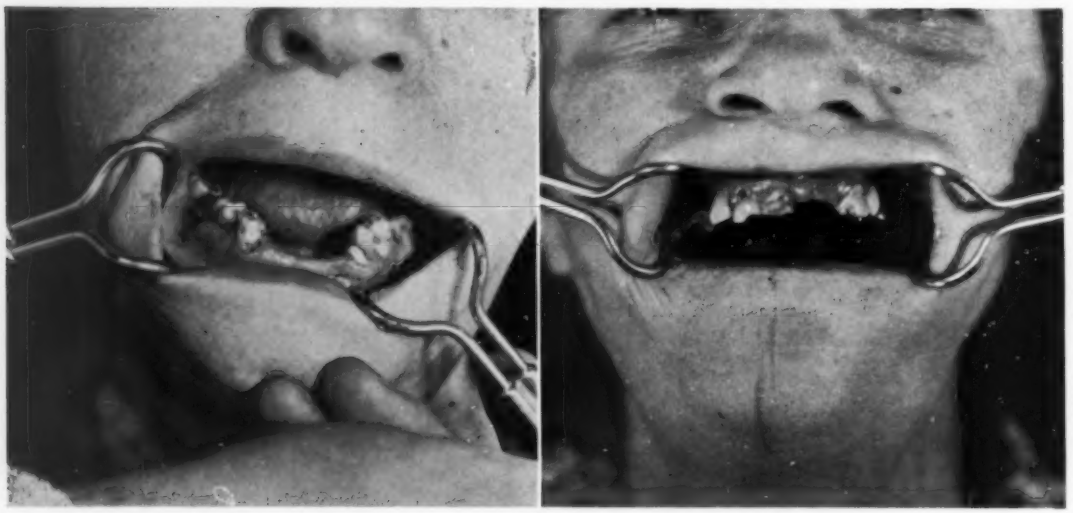

FIG. 4. Post-irradiation crumbling and demineralization of teeth.

in these locations are most likely to develop this complication. Such cases should be irradiated heavily to eliminate the soft part cancer and this should be followed by a surgical removal of the condemned section of maxilla.

(*e*) The cooperation of a skilled dentist who is acquainted with the post-irradiation, intraoral changes in soft tissue and bone is essential when the question of dentures, prosthetic appliances, dental hygiene and tooth extractions arise. The intraoral scar should be treated gently. Strong chemicals and caustics should be avoided. Recessions of the mucosa about the teeth require gentle massage. Teeth which may become decalcified should be ground down flush with the alveolar ridge and the root canals filled in an attempt to eliminate the necessity of extraction (Figs. 4 and 5). Such care is necessary as long as the patient lives.

SUMMARY

1. Roentgen and radium radiations exert a profound effect on bone and its surrounding soft tissues, especially the periosteum. The action is a direct one upon the bone cells, matrix and intraosseous blood vascular network. Secondary radiation given off by the irradiated calcium particles of

FIG. 5. Crown portions of the teeth have been removed down to a level with the gum margin. Tooth pulp has been removed and the canals filled with gutta-percha and cast base David crowns attached.

bone exerts a caustic action on the periosteum, especially its osteoblasts and capillary blood vessels.

2. Radiation sensitizes bone and definitely diminishes its resistance to infection and retards its repair after infection once has been established. Sequestration is slow and bone regeneration seldom, if ever, occurs, but healing is usually rapid after the necrotic bone has separated.

3. Three etiological factors are involved in the production of bone radionecrosis: heavy irradiation, trauma, and infection. A devitalized section of mandible may lie dormant and symptomless for years after a course of irradiation and then a severe osteomyelitis may suddenly be produced by the uncomplicated extraction of a tooth which permits the introduction of infection into the bone.

4. Complications involving the inferior maxilla are more frequent and serious than those of the upper jaw.

5. A series of 1,819 patients with intraoral cancer treated in Memorial Hospital were studied and, of these, 235 patients developed osteoradionecrosis, 13 per cent. If the lip cases are not included, the figure is increased to 20 per cent.

6. Cancers of the alveolar ridge (40 per cent) and of the floor of mouth (34 per cent are most likely to develop bone complications. In only 3.5 per cent of the lip cancers treated by irradiation was bone necrosis noted.

7. In the above mentioned series 125 patients have died and of this group osteoradionecrosis was the sole cause of death in 12 cases (9.6 per cent).

7*a*. The average period of disability suffered by patients who develop osteoradionecrosis is eleven months. The longest period of continuous osteomyelitis in our series was eight years and seven months.

8. The early diagnosis of impending osteoradionecrosis may be suspected from the symptoms and the distribution and persistence of the pain. A routine roentgenogram taken at this stage seldom shows any gross bone change.

9. Syphilis is not an etiological factor, but is of some prognostic significance.

10. When osteoradionecrosis is once established, one must be content to follow a conservative course of treatment and wait for sequestration to occur.

11. Jaw resection for bone necrosis late in the course of the disease had an operative mortality of 21.6 per cent in a series of 51 of our cases so treated.

12. The prognosis is poor. One hundred and twenty-five patients (53 per cent) have died and 16 patients are alive with cancer or cancer plus osteomyelitis. Seventy-nine patients (33.6 per cent) are active without cancer or osteomyelitis.

13. There is some experimental evidence at this time to suggest that the present divided or protracted dosage technique of roentgen irradiation may be less destructive in its action on bone tissue than were the older methods.

14. It is our hope that small circular treatment portals for roentgen therapy and the use of peroral portals whenever possible coupled with careful shielding of the mandible and soft parts when interstitial radium is used, will in the future substantially reduce the morbidity and mortality from osteoradionecrosis.

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RADIUM THERAPY IN PRIMARY CARCINOMA OF THE URETHRA*

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PRIMARY carcinoma of the urethra in the female is a rare condition. Menville and Counseller found but few cases reported in the literature and in 1935 reported a single case of mucoid carcinoma of the urethra found in their service. Meigs found this lesion but rarely in his large series of gynecological cases, and Healy reports less than 1 per cent of primary carcinoma of the urethra seen in the gynecological service at Memorial Hospital. This condition is not noted by Ewing in his book on "Neoplastic Diseases" and Pomeroy in 1936 reports observing only 7 cases in his series. Auer describes 22 cases treated by him over a period of many years. Volbracht adds 7 cases at the Women's University Clinic in Berlin to the 14 previously reported there by von Mikulicz-Radecki in 1931.

Of 625 cases of cancer of the cervix, vagina and vulva treated in the Radiation Therapy Department at Bellevue Hospital during the last ten years there were only 6 cases of cancer of the urethra.

In most instances cancer of the urethra in the female is a secondary involvement due to extension from a lesion of the vulva, vagina or cervix. The lesion may be limited to the urethral meatus, or involve the whole canal and at times extend to and involve the bladder. Inguinal glands may or may not be palpably involved. In our series, 3 cases had inguinal node extension.

Malignant involvement of the urethra, like cancer elsewhere, occurs most often in elderly women. In our comparatively small series it occurred in women in the fifties and sixties. The youngest was fifty-two and the oldest sixty-nine years of age.

Usually the symptoms are not distinctive, vaginal bleeding being the most common indication. When the tumor growth is large, severe pain may be present. In the 6 cases herewith reported 2 patients complained of vaginal bleeding—1 of vaginal discharge, 1 of pain and frequency, 1 of frequency and hematuria, and 1 of vaginal discharge with pain in the pelvis.

Of the women reported in this series 5 were married and had children.

The local lesion involved the meatus in all cases and extended along the vaginal portion into the vagina.

Diagnosis was confirmed in all cases by removal of a section of the tumor growth for biopsy. The histology was reported as adenocarcinoma in 1 case, squamous cell type carcinoma in 2 cases and plexiform type carcinoma in 3 cases.

TREATMENT

Radical surgical removal of the urethra and dissection of the inguinal nodes has been recommended for carcinoma of the urethra. Such extensive operative procedures, however, are indicated only in very early cases. Irradiation by roentgen rays and radium is a method of equal value without the associated mortality and morbidity of surgery. Except for removal of bulky tumor mass, for which we employ endothermic surgery, the method of treatment we use is a combination of roentgen and radium therapy. Treatment comprises vaginal hygiene, roentgen therapy to the inguinal nodes and radium therapy to the local lesion.

Roentgen therapy is administered to the right and left inguinal areas with high voltage roentgen rays. The factors are 200 kv., with 0.5 mm. Cu, 1 mm. Al filter, at a dis-

* Read at the Twenty-second Annual Meeting, American Radium Society, Atlantic City, N. J., June 7–8, 1937.

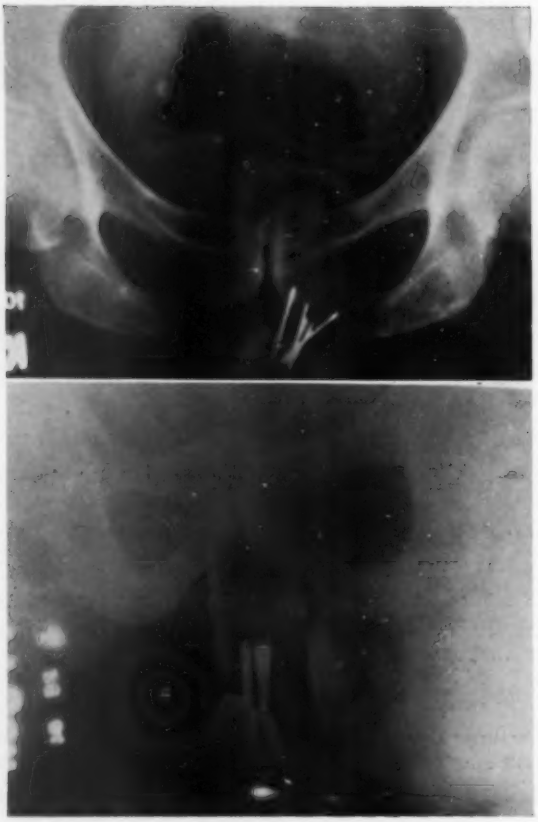

Fig. 1. Roentgenogram showing radium needles and radium tubes in place in the treatment of urethral cancer.

tance of 40–50 cm., through 9×12 cm. portals.

The method of radium therapy employed is determined by the extent of the involvement present. When the lesion is limited to the meatus, treatment is given by radium puncture with gold filtered seeds or platinum needles. The technique is carried out as follows: an indwelling catheter is first placed within the bladder, then the gold filtered seeds of 0.5 to 1 mc. radon content are inserted in and around the lesion, 500 to 1,500 mc-hr. being administered. In large tumor lesions platinum filtered needles of 0.5 mm. filtration and 25–27 mm. in length are inserted in and around the tumor and a dose of 1,000–2,500 mg-hr. is given.

When the cancerous lesion involves the whole urethra and extends through the mucosa, a sound containing radium tubes may be inserted alongside the retention catheter in the urethra. The tubes are of 5 mg. content and filtered with 1 mm. platinum. The dosage is proportionate to the size and extent of the lesion, and the amount of radiation applied externally to the urethra by the needles inserted in the surrounding tumor mass. The total dose employed does not exceed 3,000 mg-hr. distributed over the whole length of the urethra. For a large tumor growth, 6 cm. radium needles each containing 3 mg. of radium are used for the interstitial radium treatment. Another method of treatment is to construct a mold made of gauze rubber or wax which is fitted into the vaginal vault. In the mold is placed the radium filtered through 1 mm. Pt and containing 5–10 mg. of radium. Scattered radiation to the vagina may be minimized by a protection sheet of $\frac{1}{4}$ inch lead applied over the mold. The mold is retained against the urethra by vaginal gauze packing (Fig. 1).

In cases where the lesion extends to the bladder and pelvis, palliative high voltage roentgen rays are administered through the pelvis. Treatment may be given through large anterior and posterior suprapubic areas in 150 r doses for six to eight treatments administered to each area alternately at daily intervals. In cases where active therapy is planned, crossfire irradiation by high voltage roentgen rays is given, directed through the anterior and posterior right and left pelvic areas. The factors used are 200 kv., with 0.5 mm. Cu plus 1 mm. Al filter, at a distance of 40–50 cm. through fields of 9×12 cm. or 10×15 cm. Two areas per day are treated with 150 r per area at intervals of two to four days until a dose of 2,000–4,000 r is given.

Where the planned treatment is a combination of roentgen rays and radium the roentgen irradiation always precedes the radium therapy.

When complete blockage of the urethra takes place along with involvement into the bladder, surgical implantation of the ureters into the colon is advisable. The prognosis in all but the earlier cases is usu-

ally poor. Unfortunately, because of the economic status of clinic cases, follow-up for any length of time in these cases was not possible, the longest record being that of Case III observed for three years. Case reports of the 6 cases treated in our series and the results are appended.

Case I. W. J., aged fifty-six, single, gravida III; admitted March 10, 1933. Complained of vaginal bleeding and urinary leakage. Examination showed a hard bleeding polypoid growth involving the anterior lip of the urethral meatus. Inguinal nodes were not palpable. Biopsy: the histology was plexiform epithelioma. Treatment was given with high voltage roentgen rays to the right and left anterior and posterior inguinal areas; 1,000 r was administered to each area. In addition 1,400 r was delivered directly through the vaginal area. Following the roentgen therapy interstitial radium therapy was used, 10 needles 35 mm. long containing 2 mg. of radium each and 5 needles 60 mm. long containing 3 mg. of radium each were inserted in and around the tumor mass. A dose of 1,500 mg-hr. was administered. The tumor gradually receded and the ulceration healed. The case was followed for one year and the patient did not return to the clinic.

Case II. M. M., aged sixty-nine, married, gravida V; admitted August 30, 1935. Complained of vaginal bleeding. Examination showed an irregular ulceration along the vaginal portion of the urethra. There was palpable involvement of the left inguinal lymph nodes. Biopsy: the histology was squamous cell carcinoma. Treatment was begun with high voltage roentgen therapy to the left inguinal area and to the vulva. A dose of 1,500 r was given. Following roentgen therapy, a radium mold was fashioned about the lesion and fitted into the vaginal cavity. The mold contained 9 tubes of radium of 10 mg. each, filtered with 1.5 mm. Pt and a dose of 4,300 mg-hr. was administered. The lesion healed but eight months later a lymph node involvement was noted in the right inguinal area. This was treated with the 5-gram radium pack and a dose of 40,000 mg-hr. administered. Four months later a small recurrence was noted at the original tumor site and this was excised by endothermic surgery. The patient was last seen on December 14, 1936.

Fig. 2. Case IV. *A*, before treatment; *B*, after irradiation.

Case III. M. D., aged sixty, married; admitted May 23, 1929. Complained of frequency and hematuria. Twenty years previously had had an operation on the bladder and oophorectomy. Urinary urgency especially at night and hematuria for two weeks. Examination showed thickening and induration of the whole urethra. Inguinal nodes were not palpable. Biopsy: the histology was plexiform type car-

cinoma. Treatment: high voltage roentgen therapy to right and left anterior inguinal areas, 600 r to each, followed by a radium sound in the urethral canal and a surface vaginal mold applied to the urethral wall; 2,700 mg-hr. was administered. The lesion was destroyed and the patient, followed for three years, was well without recurrence.

Case iv. L. C., aged sixty-seven, married, no children; admitted January 16, 1929. Complained of vaginal discharge, moderately bloody. Examination showed a large cauliflower mass replacing the meatus and extending beyond the vulva. The clitoris was involved. Inguinal nodes were enlarged and palpable. Biopsy: the histology was plexiform type carcinoma. Treatment: high voltage roentgen therapy was administered to both inguinal areas, 600 r to each, followed by interstitial implantation of radium needles. Thirteen needles were used, 35 mm. long and containing 2 mg. of radium, each filtered through 0.5 mm. Pt and left in place to give a dose of 2,800 mg-hr. Three and six months later a second and third course of roentgen therapy was administered to inguinal areas. Patient is alive and well without recurrence of local lesion for two years (Fig. 2, *A* and *B*).

Case v. A. E., aged fifty-two, married; admitted March 27, 1934. Complained of pain and soreness in the vagina and burning on urination. Examination showed a papillary growth involving the meatus and extending to the vaginal walls. Inguinal nodes not palpable. Biopsy: histology is squamous cell type carcinoma. Treatment: high voltage roentgen therapy to both inguinal areas, 1,200 r being given each, followed by radium therapy in the form of a vaginal mold containing 6 tubes of radium, each 10 mg., filtered by 1.5 mm. Pt and left in place for ninety hours giving a dose of 5,400 mg-hr. Patient succumbed from intercurrent disease ten months later. A small local recurrence was present.

Case vi. C. D. L., aged fifty-seven, married; admitted June 27, 1932. Complained of yellow vaginal discharge and pain in the lower left pelvis. Examination showed a large red irregular mass surrounding and involving the urethral meatus and invading the vaginal urethral wall. Inguinal nodes palpable. Biopsy: the histology was adenocarcinoma. Treatment: high voltage roentgen therapy was administered to the anterior and posterior lower right and left pelvis and inguinal areas, 1,000 r given to each area, followed by interstitial radium to the local lesion. Ten needles 60 mm. long containing 3 mg. radium each, filtered through 0.6 mm. Pt and two needles 35 mm. long containing 2 mg. radium each filtered through 0.5 mm. Pt were inserted in and around the lesion, parallel and alongside the urethra. A dose of 2,244 mg-hr. was administered. The patient did poorly and died two months after treatment.

CONCLUSIONS

Primary malignant lesions of the urethra are rare. Most commonly the urethra is secondarily involved in conditions associated with carcinoma of the vulva, vagina or cervix. Only 6 instances of primary carcinoma of the urethra were encountered during the past twelve years among the 625 cases of carcinoma of the vulva, vagina and cervix treated in the Radiation Therapy Department at Bellevue Hospital.

Treatment in these cases was carried out with surgery and irradiation or irradiation alone. The case histories are reported in detail.

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DISCUSSION

Dr. David Y. Keith, Louisville, Ky. I believe it would be an error on the part of this meeting to accept the proportion of the number of cases of urethral caruncle given in this series as the correct percentage of urethral carcino-

mas in all tumors of the generative organs of the female. I am sure I have treated a great many more cases of carcinoma of the urethra than the number reported by Dr. Kaplan, and I am just as reasonably sure that my total number of cancers of the female pelvis is not as great as the total number he has used in obtaining his statistics.

Dr. Kaplan also states that his primary cases have all been advanced, which has not been our experience. We can recall cases of carcinoma of the urethra that have come in for treatment, all early carcinoma. In 1 no symptoms were present, the tumor being discovered in a check-up of college teachers by her family physician, and upon the removal of a minute piece of tissue, a diagnosis of carcinoma was made. In the other 2 early cases, symptoms were very mild and of short duration. In many of the early cases the clinical diagnosis was urethral caruncle, while the microscopical diagnosis was primary carcinoma.

I would like to see someone collect a large series of cases from various men of our clinics and see if the percentage of primary urethral carcinoma in the gynecological groups will coincide with Dr. Kaplan's percentage and prove if this percentage is correct or incorrect.

Dr. Kaplan (closing). We were very careful to select as primary carcinoma of the urethra only those cases that we could show originated in the urethra. We had a large number of vulvar cases that involved the urethra. It is not unusual to say that primary carcinoma of the urethra is of rare occurrence, for most clinics interested in that lesion are reporting the same thing. Healy says it occurs in less than 1 per cent in their cases. Meigs says there were very few in his service in the Massachusetts General Hospital and Pomeroy reported only 7 cases. I think real primary carcinoma of the urethra is rare.

The dose used is large because, as we see these cases, the lesion is extensive and we think a large dose is necessary to control it.

THE ROENTGENOLOGIC LOCALIZATION OF TUMORS AFFECTING THE SPINAL CORD*

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THE observations recorded in this paper cover the author's experience in the roentgenologic localization of 198 verified tumors affecting the spinal cord that were operated on at The Mayo Clinic during a period of five years ending January, 1936. The fundamental roentgenologic criteria used in this series were not significantly different from those which I have previously reported[1,2,3,4,8] and they therefore will not be discussed in detail here. Of more importance, I believe, are certain additional observations which reflect the present efficiency of roentgenologic procedures in the localization of these lesions.

In our experience at The Clinic, the number of tumors affecting the spinal cord that come to operation is increasing each year, and of no little significance is the fact that the average size of these tumors is considerably smaller than formerly. This reflects in no small way the increasing accuracy of the clinical diagnosis of these lesions, and also the fact that clinicians everywhere are becoming more conscious of tumors of the spinal cord. In keeping with the fact that tumors of the spinal cord are being diagnosed and operated on earlier is the evidence that only 30.3 per cent of the lesions in this group were large enough to provoke secondary erosion in contiguous vertebrae sufficient to permit direct roentgenologic localization of the lesion.

For roentgenologic consideration, tumors affecting the spinal cord may be classified as follows: (1) benign tumors arising from soft tissues within the spinal canal, (2) malignant tumors arising from soft tissues within the spinal canal, and (3) protrusions and tumors of the intervertebral disc involving the spinal canal.

All benign tumors involve the vertebrae in a similar manner, that is, by erosion from pressure. They have no individually distinguishable roentgenologic characteristic except the neurofibromas, which have a tendency to extend through an intervertebral foramen and thus produce an hour-glass tumor partly within and partly outside the spinal canal. The margins of the eroded area are sharply demarcated and coincide with the surface of the tumor or displaced spinal cord.

Malignant tumors arising from soft tissues within the spinal canal include both primary and metastatic lesions. The intramedullary tumors, particularly the gliomas with the exception of ependymal cell gliomas of the filum, do not commonly involve the vertebrae secondarily (12.5 per cent). Primary or metastatic malignant tumors of the dura or soft tissues contiguous to it invade the surrounding vertebral parts and produce the well known roentgenologic image of malignant disease of bone.

Tumors, and particularly protrusions due to trauma of the intervertebral discs, frequently involve the spinal canal and produce symptoms by compressing the spinal cord or contiguous nerve roots. In the traumatic variety the intervertebral space may be narrowed, but not necessarily so, and this change therefore cannot be depended on for the localization of such lesions. In the great majority of cases the diagnosis is dependent on the use of some contrast agent, especially radiopaque oil, in the subarachnoid space, to localize the site of the protrusion.

For practical purposes the roentgenologic signs of tumors affecting the spinal cord may be classified as direct and indirect. The direct signs consist of changes

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

in the surrounding vertebral structures due to erosion from pressure by the tumor or actual infiltration by it and calcification within the tumor. The indirect signs are those observed after the introduction of a contrast agent, especially radiopaque oil, in the intraspinal subarachnoid space.

DIRECT SIGNS

In Table I it will be observed that the extradural tumors, which constitute about 25 per cent of all true tumors affecting the spinal cord, produced secondary changes in the vertebrae at the site of the lesion which was recognized by the roentgenologist in 47.2 per cent of the cases. The intradural, extramedullary tumors, which make up approximately 50 per cent of tumors affecting the spinal cord, produced roentgenologic changes in the contiguous vertebral structures in 21.6 per cent of the cases. The incidence of vertebral changes occurring with intramedullary tumors varied greatly, depending on their location above or below the conus. In the former group only 12.5 per cent produced changes in the surrounding vertebrae, whereas in the filum, the ependymal cell gliomas provoked recognizable changes in 80 per cent

TABLE I

TUMORS OF THE SPINAL CORD

Type	Cases	Changes in Bone	
		Cases	Per Cent
Extradural	53	25	47.2
Intradural	111	24	21.6
Intramedullary	24	3	12.5
Filum	10	8	80.0
Total	198	60	30.3

of cases. The average for all groups indicates that approximately 30 per cent of all tumors affecting the spinal cord produced changes in the structures of the contiguous vertebrae that could be recognized by the roentgenologist.

As shown in Table II, the incidence of changes in bone varies greatly with the cytology of the tumor. The most common tumor, the neurofibroma, produced changes in the surrounding vertebrae in 44.4 per cent of the cases, whereas the meningioma, another frequent type of tumor, produced changes in the vertebrae in only 9.3 per cent. In addition, two meningiomas were calcified sufficiently to be recognized in the

TABLE II

CLASSIFICATION OF TUMORS

	Cases	Changes in Bone	
		Cases	Per Cent
Neurofibroma	54	24	44.4
Meningioma	43	4	9.3*
Intramedullary:	24	3	12.5
Filum ependymal cell	10	8	80.0
Hemangioma and hemangio-endothelioma	14	3	21.4
Lipoma	3	3	100.0
Prolapsed disc	11	4†	36.3
Inflammatory lesion	8	0	0

* Calcified in 2 additional cases (13.9 per cent).
† Narrowed intervertebral space.

roentgenogram. It is significant that 80 per cent of the filum ependymal cell gliomas caused erosion of bone, and since this tumor constitutes 66 per cent of all tumors of the filum, its presence should be suspected when erosive changes can be observed in the lumbar vertebrae or sacrum. It is curious that 100 per cent of the lipomas provoked vertebral changes, and one of these tumors was intramedullary in location. It is also noteworthy that no case of inflammatory disease of the cord or meninges produced secondary changes in the surrounding vertebrae.

In 1933 Elsberg and Dyke[7] called attention to the value of measuring the horizontal distance between the mesial borders of vertebral pedicles at the same level as an aid in the recognition of erosion of the pedicles and enlargement of the spinal canal at the site of an expanding intraspinal lesion. By plotting these measurements on a chart, showing curves for the usual and maximal normal interpedicular distances, they were able to demonstrate

an increase in the interpedicular distance at the level of the lesion in 42 per cent of a series of 67 cases of tumor of the spinal cord. In 79 per cent of the cases in which there was a pathologic increase in the interpedicular distance, a flattening of the pedicles, which I have emphasized as an early sign of tumor affecting the spinal cord, occurred. Since early erosion of the pedicles may be difficult for the less experienced examiner to recognize, routine measurement of the interpedicular distances in cases in which a tumor of the spinal cord is suspected will undoubtedly result in the identification of certain tumors that otherwise would be overlooked.

I cannot agree, however, with the conclusion of Elsberg and Dyke that flattening of the pedicles is of pathologic significance only if the interpedicular distance is increased at the same level, because in a recent series of 55 cases in which the tumor was localized by the roentgenologist on the basis of erosion of the pedicles, with or without coexistent erosion of the laminae or bodies of the vertebrae, the interpedicular distance at the level of the tumor was within normal limits in 25 cases (45.4 per cent). In the case of dumb-bell neurofibromas, measurements of the interpedicular distance may be misleading, since in these cases the tumor produces erosion of the superior or inferior surfaces of a contiguous pedicle without alteration, in some cases, of the true horizontal interpedicular distance. In a group of 79 tumors in which no vertebral erosion could be identified by the roentgenologist, the interpedicular distance was normal in 74, or 93.6 per cent of cases. In 5 cases, or 6.3 per cent, there was evidence of increased interpedicular distance at the site of the tumor without erosion of bone that was recognized by the roentgenologist. This point emphasizes that a small percentage of spinal cord tumors may be localized by the roentgenologist before bony erosion is evident if the Elsberg and Dyke charts are used routinely. On the other hand, however, in a much greater percentage of cases (45.4) the tumor was localized by the roentgenologist because of contiguous bony erosion when the interpedicular distance at the same level was normal. Hence a large percentage of error may occur if one depends on the measurement of the interpedicular distance alone for the localization of a tumor.

In the past it was generally believed that when a tumor was large enough to erode a contiguous vertebra, complete or partial block of the cerebrospinal fluid existed. Our recent studies indicate that in 25 cases in which there was vertebral erosion the cerebrospinal fluid was completely blocked. In 9 cases the cerebrospinal fluid was partially obstructed. In both of these groups the serum protein of the cerebrospinal fluid was higher than normal. In 10 instances, however, in which erosion of the vertebrae was evident, there was no obstruction of the cerebrospinal fluid, and in 8 of these instances the serum protein of the cerebrospinal fluid was normal. It is evident, therefore, that the direct roentgenologic evidence may be more significant than studies of the cerebrospinal fluid in about 6 per cent of cases of tumors affecting the spinal cord.

INDIRECT SIGNS

Whenever the presence or location or extent of a tumor cannot be definitely determined by the usual neurologic or roentgenologic examinations, its presence may be revealed by the injection of a radiopaque oil into the subarachnoid space. This procedure is being used with increasing frequency to facilitate the early diagnosis of tumors within the spinal canal before compression of the spinal cord and involvement of the contiguous vertebrae have occurred. With modern technique,[1,3,4,8] small tumors are easily localized by means of a filling defect long before complete obstruction of the cerebrospinal fluid has occurred. In the majority of cases the defect is so characteristic that the extradural, intradural, or intramedullary location of the tumor can be readily determined. The procedure is contraindicated in frank inflammatory dis-

ease because of the more or less irritative properties of the oil. However, in selected cases this disadvantage is more than outweighed by the valuable information disclosed by its use.

In 1919 and 1925 Dandy[5,6] called attention to the use of air in the subarachnoid space as a means of localizing tumors affecting the spinal cord. The advantage of air over oil is that it is quickly absorbed and is nonirritating. The principal disadvantage is that, in localizing the level of a tumor, the air shadow is far less sharp than that of a radiopaque oil, and the roentgenograms must be of excellent quality and carefully scrutinized in order to be of any value. In the cervical and upper thoracic portion of the spinal column the use of air is of limited value because of the superimposed shadow of the air-filled trachea in the anteroposterior view. Dandy also suggested that tumors in the caudal area might be shown by elevating the pelvis. The use of air, however, in the subarachnoid space was not generally taken up because of the obvious disadvantages of the procedure and the more dependable information that could be obtained by the use of radiopaque oil.

The value of lipiodol in the exact localization of tumors affecting the spinal cord is emphasized by the fact that, during the past five years, we have used this method of examination with increasing frequency, and it was used to determine the presence and localization of the lesion in 37.3 per cent of the cases in which operation was performed. The accuracy of the procedure is indicated by the fact that, in this group, it localized the lesion in 72 instances with but 1 error. These statistics do not include a more recent series of 100 cases of verified intraspinal protrusion of one or more intervertebral discs in which lipiodol within the subarachnoid space played a predominant rôle in the localization of the lesion in all cases.

Within the past year or two the irritating properties of lipiodol have again been questioned because of the increasing use of this agent as a result of the current interest in intraspinal protrusion of the intervertebral discs. A revival of the use of air in the subarachnoid space, with the patient in an exaggerated Trendelenburg position, has been suggested as a means of localizing intraspinal protrusion of the intervertebral discs in the lumbar area, and I understand that this procedure is being tried in some clinics. Undoubtedly it will serve to localize large protrusions and large tumors, but I cannot fully subscribe to the use of air in the subarachnoid space because the localization of small tumors, and particularly of multiple lesions, is difficult enough with lipiodol without introducing the added disadvantages of air. In the interests of early diagnosis, and therefore of better surgical results, we should strive to improve our diagnostic acumen rather than to jeopardize it, and until a more satisfactory radiopaque substance than lipiodol is developed, I am inclined to agree with Dandy who has said that, "for localization of tumors that are known to be present lipiodol is far superior to air, and moreover, an inferior roentgenogram will make a better localization with the use of lipiodol than the best roentgenogram after the injection of air."

SUMMARY AND CONCLUSIONS

The data compiled in this series of 198 cases of verified tumors affecting the spinal cord indicate that in 30 per cent of the cases the lesion was localized by the roentgenologist on the basis of osseous changes in the vertebrae that were revealed in plain roentgenograms (direct signs).

In 37.3 per cent of the cases the lesion was localized by means of the subarachnoid injection of lipiodol, with an accuracy of 98.6 per cent (indirect signs).

While there is a slight overlapping when the lesions revealed by these signs are considered collectively, in at least 60 per cent of the cases the diagnosis and exact localization of the lesion were predominantly established by roentgenologic methods.

More recent and unpublished observations concerning the accuracy of the indi-

rect roentgenologic signs (lipiodol) in the diagnosis and localization of protruded intervertebral discs, which are playing a greatly increasing rôle in the incidence of intraspinal lesions, will significantly augment these percentages and firmly establish the roentgen ray as a major diagnostic agent in the diagnosis and localization of lesions affecting the spinal cord.

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ACCIDENTAL EXTRAPLEURAL PNEUMOTHORAX

ROENTGENOGRAPHIC APPEARANCE

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OLIVE VIEW, CALIFORNIA

WITH the more intensive collapse therapy program which has been in effect in the treatment of pulmonary tuberculosis during the past ten years, complications of treatment comprise a share of the responsibility for diagnosis placed upon the roentgenologist. Among such complications there is one only recently described by Lowys,[1] and by Davy and Rolland[2]—accidental extrapleural pneumothorax. This is a condition in which the parietal pleura, lining the thoracic cage, has been partially stripped from the chest wall in the course of initiating or maintaining an induced intrapleural pneumothorax. The exact cause has not yet been determined. Lowys, and Davy and Rolland assume that introduction of air with the point of the needle immediately external to the parietal pleura can cause its separation from the chest wall. Another possibility comes to mind, however, i.e., that the separation may be started by the injection of anesthetic solution in a plane external to the parietal pleura, and continued or enlarged by introduction of air into the extrapleural pocket thus created.

Lowys reports one case in which the pleura was first very slightly stripped by the introduction of a trocar for thoracoscopy. Later, a larger separation was caused by a pneumothorax refill. Davy and Rolland present 3 cases in which the extrapleural pocket occurred during pneumothorax refills.

Independent of the above observations, 15 instances of accidental extrapleural pneumothorax, among over four hundred pneumothorax cases, have been observed during the past year at the Olive View Sanatorium. Recognition of the first case, roentgenographically, followed a thoracoscopic observation by Dr. Charles M. Miller. The roentgen findings in this case were so clear-cut and definitive that the other cases could be recognized at first glance.

The complication occurs only in patients in whom pneumothorax has been instituted comparatively recently, or in whom the pleura has not been thickened by inflam-

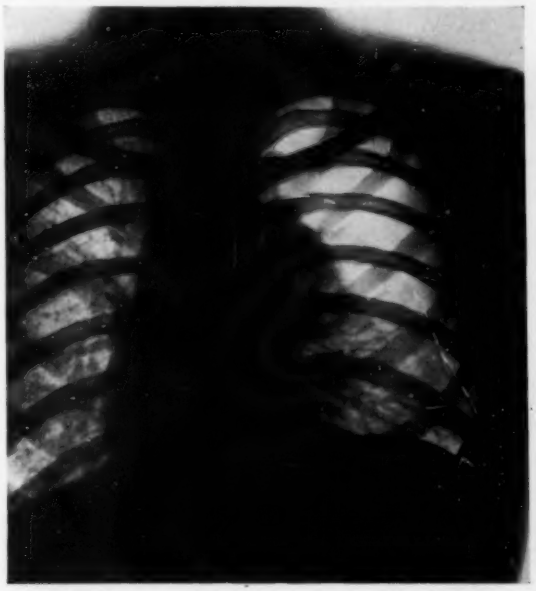

FIG. 1. Fairly extensive accidental extrapleural pneumothorax pocket, indicated by arrows, in lower part of left pleural cavity, complicating a successful intrapleural pneumothorax, indicated by dotted line.

matory change. The usual clinical symptom observed is a "tight" feeling, occasionally with moderate pain, which often persists a week or two after the refill causing this pleural stripping. There are interesting manometric findings in that an unusually small amount of air causes a positive reading, whereas the patient had previously taken average refills with a negative reading. Without a knowledge of what has oc-

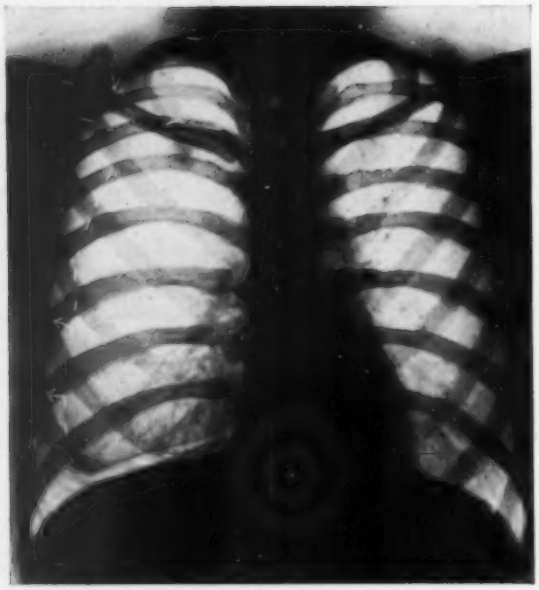

Fig. 2. Accidental extrapleural pneumothorax pocket along right chest wall. There are two such pockets, which may communicate. Very satisfactory intrapleural pneumothorax.

curred, these findings are puzzling and might presumably be the cause of untimely abandonment of pneumothorax, as suggested by Davy and Rolland.

The roentgenographic appearance is that of a very fine, sharply defined, white line, representing the parietal pleura, which starts and ends at the chest wall and circumscribes between itself and the chest wall, a long, irregularly crescentic or fusiform area of the same density as the intrapleural pneumothorax, mesial to this line (Figs. 1 to 3). If the pocket happens to be in apposition to the anterior or posterior chest wall, the pocket presents a crinkled, lacy, loculated appearance in the routine posteroanterior view. An oblique view will bring the pocket into profile. The stripping occurs in the region where pneumothorax refills are given, usually in the axilla. The extent, depending upon the amount of air injected, varies from a small bleb to an area extending from the apex well toward the diaphragm, with 2 to 3 cm. separation from the chest wall. At times, the extrapleural pocket is limited in its extension along the chest wall by an area where there are adhesions between the visceral and parietal pleura, and between the latter and the endothoracic fascia. The air may collect in greater amounts proximal to such an adhesion (Figs. 4 and 5). The extrapleural pockets usually absorb in two to three months. The persistence in some patients for nearly a year is probably explained by entrance of the needle and further introduction of air into the pocket at intervals.

The appearance can hardly be confused with adhesions. Here, the margin of the lung dropping from the chest wall between adhesions may outline a similarly shaped area, but mesial to this line there is either opaque, collapsed lung or aerated lung showing lung markings, while in accidental extrapleural pneumothorax there is either a clear area between the line representing the parietal pleura and that representing the margin of the lung, or, with less collapse, these two lines may cross each other. At times, when the lung becomes diffusely adherent to the anterior or posterior chest wall, the edge of the lung creeps out near the lateral chest wall and may cause a somewhat similar appearance. But here again,

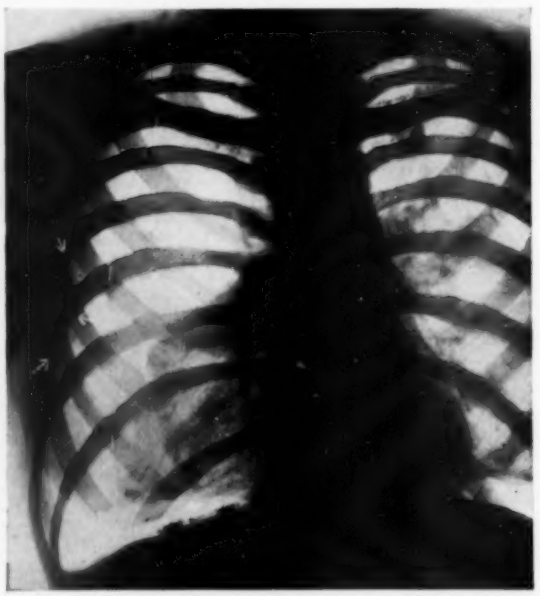

Fig. 3. Small localized accidental extrapleural pneumothorax pocket or bleb along lateral chest wall.

there are lung markings mesial to the line representing the adherent margin of the lung.

This complication of induced intrapleural pneumothorax is apparently not a serious one, but it explains a phenomenon which has undoubtedly caused some confusion in the minds of operators confronted by the manometric changes described, and,

Fig. 4. Rather extensive accidental extrapleural pneumothorax pocket extending from the axillary region nearly to the clavicle. A number of band adhesions limit the further dissection of the parietal pleura by the air. These blebs of air so hid the point of attachment of the adhesions to the chest wall as to prevent their section. The intrapleural pneumothorax is ineffective with several patent cavities.

Fig. 5. Same film as in Figure 4 nearly full size to show the details of the extrapleural pneumothorax pocket and relation to adhesions.

on the other hand, of the roentgenologist, who is, perhaps, without any knowledge of the clinical facts in the case.

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TUMORS OF THE HYPOPHYSIS CEREBRI*

FROM A ROENTGENOLOGIC VIEWPOINT

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NEW YORK CITY

THE hypophysis cerebri has been termed "the leader of the endocrine orchestra," and very aptly so, for as time goes on, it is becoming more and more apparent that practically all of our bodily functions are directly or indirectly the result of a "wave" from the baton of this all powerful leader.

The pituitary gland and the entire hypothalamic region constitute such a complicated anatomical study that the ancient anatomists were entirely baffled by its complexities. Galen made a serious attempt to disentangle this complex portion of our anatomy, but he too was finally compelled to simply call the region the plexus retiformis, the seine-like net. This was later called the rete mirabile by Galen's Latin followers, which means "the wonderful net." The region was likened to a net because the opinion then held was that the phlegm or pituita, one of the body humors, was in some way formed from the ventricular fluid by passing through this "net." Even up to the reign of Queen Anne, it was thought that the excreta of the brain was eliminated by way of the phlegm. It was this quaint belief that stimulated, if it did not actually lead to the use of snuff to promote sneezing, in order that the brain might be cleared. (These tales are much more completely told by Nieuwenhuis and also by Cushing.)

Nearly all the textbooks describe the development of the pituitary body as an ectodermal outpouching from the diencephalon, thus forming the posterior or neural portion, and an outpouching of the same germinal layer from the pharynx (Rathke's pouch) which forms the anterior or glandular lobe. This comparatively simple conception of the formation of the pituitary body is, as pointed out by Tilney, inadequate to explain its complex makeup. He describes in a very convincing manner the formation of three divisions of the anterior or glandular portion which are designated as the pars tuberalis, the pars infundibularis and the pars distalis, while the neural lobe consists of four parts, the median eminence of the tuber cinereum, the infundibulum, the infundibular stem, and the infundibular process. Thus it can readily be seen that if, as seems highly probable, each of these portions of the pituitary body has a distinct function of its own, the combinations for good or bad are extremely numerous, and as yet they are imperfectly understood. In fact, even though our knowledge is rapidly increasing, we might well borrow Galen's conception and call it the "corpus mirable."

When attempting to evaluate conditions and changes seen in the roentgenograms of the skull, and to decide whether or not they may indicate some malfunction of the pituitary, we should bear in mind not only the general architectonics of the gland, but also its cellular makeup. The average pituitary body measures roughly about $6 \times 10 \times 13$ mm., and the anterior portion is on the average at least four times the size of the neural or posterior portion. The anterior portion is made up of 52 per cent of chromophobe cells which are without granules and do not stain well, and 48 per cent of chromophile cells which do stain well. These chromophile cells may be divided into two groups, the eosinophiles and basophiles. There are about three times as many of the former as there are of the latter, and their names clearly indicate their staining characteristics. The small neural portion consists almost entirely of cells which Bucy has termed pituicytes. These are modified forms of neuroglial cells and are held to-

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gether by connective tissue, through which course many small unmyelinated nerve fibers.

The early recognition of pathology of the pituitary body and its adnexa is based not only on the variations from the normal as seen in the roentgenogram, but by correlating these changes with every other known fact relative to the patient. It must be clearly understood that the roentgen examination is not all sufficient, something set apart on a pedestal. It is part of the physical examination and forms a unit of the "jig-saw puzzle" of the patient's condition. True, the roentgen examination often forms the "keystone" and is the deciding factor of the diagnosis, but we must never lose sight of the fact that we are primarily clinicians and secondarily clinical roentgenologists. In addition, an examination of the skull, to be adequate, should consist of stereoscopic films of good technical quality, taken from many angles. We are still plagued on every hand by most inadequate examinations.

Before considering the several variations from the normal which we have come to associate with pituitary disease, let us briefly mention a few rather well-established facts regarding the hypophysis which may help in evaluating the changes seen in the film.

Fig. 1. Chromophobe pituitary adenoma showing a typical "ballooned" sella turcica.

Fig. 2. A case of a large chromophobe pituitary adenoma which has enlarged the sella turcica. The dorsum sellae is atrophic and pressed backward. The tumor has grown out of the sella turcica and displaced the pineal body backward.

It is indeed rare to find a primary tumor of the pituitary body arising anywhere other than in the anterior lobe or the pars tuberalis, and it is well to remember that the pars nervosa or posterior lobe probably does not give rise to primary tumors but may be the site of a malignant metastasis. Strange as it may seem, the chromophobe cell, predominant though it is, is evidently almost if not entirely inactive as far as the production of hormones is concerned. But according to the studies of Biggart and Dott, the chromophobe cell is the mother cell from which the active chromophile cells originate. This accounts for our finding tumors of the mixed type; in fact, most large chromophile tumors will be found to contain large numbers of transitional eosinophile cells.

Many pituitary tumors never develop beyond the microscopic stage. This is particularly true of the basophilic variety. Hence it is readily seen that in many in-

Fig. 3. Chromophile pituitary adenoma. The sella turcica is somewhat enlarged and there is slight thickening of the bones of the vault with enlargement of the frontal sinuses.

stances we must seek elsewhere than in the sella turcica for evidences of the presence of such tumors. On the other hand, hypophyseal tumors may grow to great size and occupy most of the interpeduncular space, even in rare instances invading the adjacent structures.

We are no longer content merely to state from our examination that a pituitary tumor is present, but must go a step further and indicate the histologic type. This is not an infrequent possibility when all factors are carefully considered. Tumors of the hypophysis cerebri are not uncommon. They constitute a somewhat variable proportion of all intracranial tumors depending upon the clinic, but a general average would be about 18 to 20 per cent. Of these, about 70 per cent would be tumors composed almost entirely of chromophobe cells, about 25 per cent would be predominantly chromophilic, and about 5 per cent could be classed as definitely mixed or transitional in type. These percentages are of necessity open to slight variations because the personal equation is somewhat a factor when classifying the mixed tumors. As is well known, the chromophobe adenoma gives rise to hypopituitarism, while the chromophile type produces hyperpituitarism resulting in either gigantism or acromegaly, depending upon whether or not the epiphyses have closed. The basophilic tumor is rare and gives rise to Cushing's syndrome. This syndrome can also be caused by tumors of the adrenal glands, the ovaries, and the thymus. It is uncommon to find a pituitary adenoma in a patient under fifteen years of age.

The diagnosis of the presence of a pituitary adenoma in its early stages often presents serious difficulties. It is here that the history plays an important rôle. The tumor may be so small that the changes in the sella turcica are not evident, and in fact not infrequently our best efforts will fail to provide a definite diagnosis. The tumor may remain dormant as far as growth is concerned, but be able to produce an endocrinopathy. This may lead to the acromegaloid type of skull, with the rather prominent frontal sinuses developed an-

Fig. 4. Chromophile pituitary adenoma showing considerable enlargement of the sella turcica. The enlargement suggests the presence of a tumor of the mixed type.

teriorly and not at the expense of the cranial capacity, and heavy facial bones but no prognathism. The tables of the calvarium will be well defined, with the inner and outer tables thin, while the middle or diploic portion will be relatively large, although the entire vault may be no thicker than the average. The calcium content of the bones may be seen to be lessened, due to the proportionately large amount of diploe, but on careful examination the inner and outer tables will usually appear quite dense. There will be no evidence of increased intracranial pressure and the sella turcica may be of average or large average size, but with a rather dense cortex. This cortical density may be found in the presence of a tumor which has ceased to enlarge, and is probably due to a regenerative attempt on the part of the bone. The early and small tumors will not give rise to any visual disturbances, but headaches may be a factor, often occurring in the occipital region. Such variations in the general appearance of the skull would be compatible with a chromophile eosinophilic type of adenoma. The appearance of the sella turcica alone, however, would be equally compatible with a small chromophobe tumor.

Inasmuch as no two skulls are exactly alike, it is indeed a pity that each of us cannot have films taken of our heads shortly after puberty, for purposes of comparison. How much easier it would be, with such films available, to recognize early evidences of pathology.

Fig. 5. Basophilism. Note the granular appearance of the bones of the vault and base.

Fig. 6. A craniotuberal cyst with some calcification above and behind the sella turcica, and evidence of a considerable increase of intracranial pressure.

In the presence of an adenoma which is gradually enlarging, we will see an evident demineralization of the cortex of the inner portion of the dorsum sellae and posterior clinoid processes. These are the first structures to undergo halisteresis. As the tumor enlarges, the sellar floor will show similar loss of bone calcium, and lastly the tuberculum sellae and anterior clinoid processes will become involved. This is due to some protection of these structures by the attachment of the diaphragma sellae which must be stretched or even ruptured before the tumor can exert much pressure on them. Before the tuberculum and anterior clinoids become involved we would probably find the sella turcica to have undergone expansion and to have assumed the form so well described as "ballooning." This is usually the last stage of the purely intrasellar adenoma. As the tumor enlarges and finally bursts the confines of the sella turcica, this structure will lose its charac-

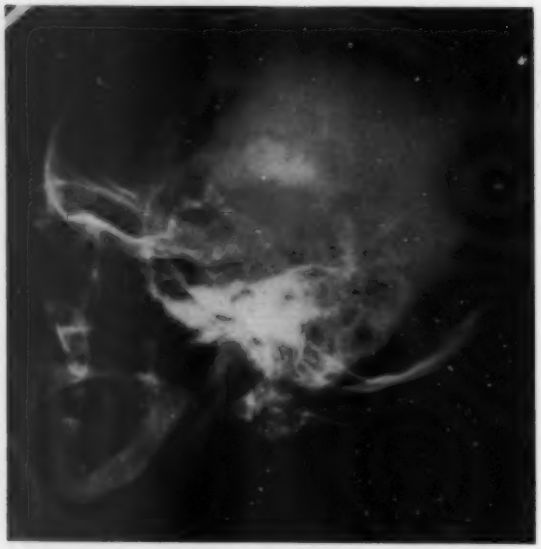

Fig. 7. A craniotuberal cyst with a large irregular deposit of calcium in the cyst wall.

teristics entirely, and only portions of its various components remain visible as thin spicules of bone. Not infrequently a large tumor may decompress the sella turcica by bursting into the sphenoid sinuses.

Thus it becomes evident that by a study of the involvement of the various structures forming the sella turcica we may be able to form a rough estimate as to the approximate state of the growth of the tumor. In addition, if we bear in mind the fact that the chromophobe tumor gives rise to no bony growth changes, whereas the chromophilic type does, and that the chromophobe tumor is usually much the larger of the two types, we can, with a fair degree of accuracy, state the type of tumor present.

The mixed type of adenoma is not easy to recognize from the roentgenogram because one form of cell may well be predominant, and so give rise to the fairly characteristic changes usually associated with the differentiated types. If, however, we find a definite acromegalic change and the sella turcica indicates the presence of a large tumor, we may well suspect the presence of a mixed type of tumor because the chromophile adenoma is not apt to be very large and yet the bony changes clearly indicate the presence of active chromophile cells. The basophilic adenoma is relatively uncommon and as it is usually very small there will rarely be any change in the configuration of the sella turcica. But there will be, if the tumor is active, a very irregular halisteresis of the vault, and to a somewhat less extent the bones of cartilaginous origin; the basic bone structure, however, is unaltered. This halisteresis will give the bones a rather granular "pepper and salt" appearance not unlike that often associated with hyperparathyroidism and occasionally with adrenal tumors; in fact, it may well be that a differentiation from an examination of the films alone would not be possible. Pituitary adenomas are not infrequently found to be undergoing some form of cystic degeneration.

Malignant tumors may occasionally involve the pituitary body. These are usually adenocarcinomas. Such a tumor involving the basophilic cells has been reported which gave rise to Cushing's syndrome. As a rule, the history will reveal a rapid progress of symptoms in the case of an adenocarcinoma as compared to the slow progress of an adenoma. The sella turcica will show marked destruction due at times to actual invasion of the bone so that the structures will be entirely destroyed. This in contra-

Fig. 8. A large craniotuberal cyst with calcification in its walls. The tumor extends far above the greatly enlarged and atrophic sella turcica.

distinction to the slow absorption of the bone due to pressure from an adenoma, in which case we can usually see spicules of bone remaining even after considerable absorption has taken place. There frequently comes a time in the progress of pituitary tumors of all types when the sella turcica is so completely destroyed that we must rely almost entirely on the history and physical findings to make a differential diagnosis.

There are several lesions which must be thought of as possibilities when considering the differential diagnosis of a strictly pituitary lesion. At the very outset, one should have clearly in mind the fact that only about 2 or 3 per cent of pituitary tumors ever grow in such a manner that they give rise to an elevation of intracranial pressure. Hence, if such a condition is recognized the chances are small that the lesion will prove to be a pituitary adenoma. Also it should be remembered that rarely will a pituitary adenoma calcify, and that every enlarged and atrophic sella turcica by no means indicates the presence of a pituitary tumor.

Before discussing the differential diagnosis, let us take up the cystic tumors which

Fig. 9. A craniopharyngioma or bucconeural pouch tumor. Note the calcification above and in the enlarged sella turcica.

Fig. 10. Frontal astrocytoma containing streaky calcification. Note the atrophy and "ballooning" of the sella turcica which without the calcification might easily be confused with the changes caused by a pituitary adenoma. (Compare the sella turcica of this case with that shown in Fig. 1.)

must be included in any consideration of pituitary lesions. These tumors have been termed craniopharyngiomas, Rathke's pouch cysts, bucconeural cysts, adamantinomas, hypophyseal duct tumors, and by several other names. Bailey thinks of them as epitheliomas. They are essentially congenital and therefore chiefly found in children, although one patient in our group of cases was in his sixth decade. This form of tumor constitutes between 4 and 5 per cent of all intracranial tumors. The tumors arise from squamous epithelial rests, and, according to Tilney and others, should be divided into two groups: those arising from the tuber cinereum and those originating in true vestigial remains of Rathke's pouch in the anterior pituitary lobe. The former, which are far more common, might be termed craniotuberal epitheliomas, and the latter craniopharyngiomas. Both types are very apt to be cystic and large, so large in fact that they may block the interventricular foramen and raise the intracranial pressure, and in addition press backward on the mid brain so that cerebellar signs may be produced. Such a complication occasionally makes the diagnosis difficult, because due to direct pressure on the hypothalamus, complicated symptomatology may result.

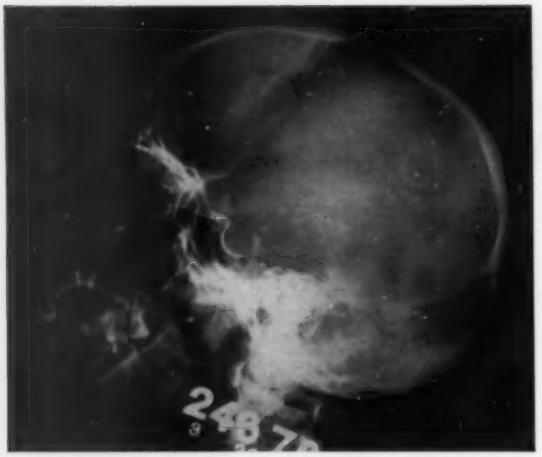

Fig. 11. Calcification in a right temporal astrocytoma. There is slight enlargement of the sella turcica and atrophy of the dorsum sellae, not unlike the changes caused by a small intrasellar adenoma.

It is not uncommon to find the patient, if a child, presenting the characteristics of Fröhlich's syndrome.

In the roentgenogram we could hardly hope to be able to differentiate definitely between the tumors originating from the tuber cinereum and those from the body of the hypophysis. But if one remembers that the tumors originating in the hypophysis are relatively rare, an inaccurate diagnosis will be uncommon. Fortunately about 80 to 90 per cent of these cystic tumors calcify sufficiently to cast a shadow on the roentgen film. The deposits will usually be punctate or linear or a combination of the two forms and be situated in the sella turcica or in and above it. Rarely the calcification will be found at some distance from the sella turcica; when so found the patient is more apt to be an adult, and the deposit may be so formed that a cyst is strongly suggested. Evidences of increased intracranial pressure are a frequent accompaniment of these tumors when they occur in children, and consist of atrophy of the inner table of the vault with or without a deepening and increase in number of the convolutional impressions, and slight or marked atrophy and distortion of the sella turcica; this structure may at times be totally uninvolved and the diagnosis rest entirely on the finding of deposits of calcium and the clinical history. It might be noted here that when such a tumor occurs in an adult, evidences of increased intracranial pressure usually do not appear until relatively late in the course of the lesion's growth. In short, if we find calcification directly above and perhaps in the sella turcica, whether the patient be child or adult, we should strongly suspect the presence of a craniotuberal epithelioma or craniopharyngioma.

Now let us consider some of the more common lesions which have to be thought of when making a differential diagnosis of pituitary tumors. First of all, we must not forget that multiple lesions are not impossible, and, although extremely rare, such a possibility is not to be ignored. The suprasellar meningioma may give rise to symptoms very similar to the pituitary tumor. It is, however, not common for a meningioma in this position to produce any visible changes in the sella turcica. Such a tumor not infrequently arises from the tuberculum sellae and so may give rise to slight or marked cortical hypertrophy. When such a change is recognized it is almost pathognomonic. Not infrequently this type of tumor will confuse us completely and to make the

Fig. 12. The atrophy and enlargement of the sella turcica are due to the presence of a chordoma.

diagnosis we must turn to encephalography. A good encephalogram, taken in the upright position, will usually permit of a fairly complete portrayal of the basal cisterns. In the presence of a suprasellar meningioma we would expect to see a moderate distortion, probably backwards, of the cisterna lamina terminalis, a flattening or lack of filling of the cisterna chiasmatis and perhaps a distortion of the anterior portion of the cisterna interpeduncularis. If the lesion were intrasellar, we would expect to see only a variable degree of arching upward of the diaphragma sellae as outlined by gas in the cisterna chiasmatis.

A small glioma of the optic chiasm may present a serious problem in differential diagnosis. Here again, the sella turcica may be practically uninvolved, but the eye symptoms and findings will be very suggestive, and out of all proportion to the changes in the sella turcica if such symptoms were to be ascribed to a pituitary tumor. In addition, the optic foramina may well show unilateral or even bilateral enlargement. It is true that occasionally we find an optic foramen enlarged by a pituitary adenoma, but not until the sella turcica shows considerable involvement. Not infrequently encephalography will be necessary to arrive at a certain diagnosis. But in the presence of an optic chiasm glioma, the distortions of the basal cisterns will not differ greatly from those produced by a suprasellar meningioma; however, the history and clinical findings coupled with the encephalographic findings will make the diagnosis. Rarely a chiasmal glioma will undermine the anterior clinoids. This would not be expected in the presence of a meningioma.

A rather rare tumor which can at times produce confusing changes is the chordoma. This tumor originates from a remnant of the notochord occasionally found on the clivus, which goes by the name of the ecchordosis physaliphora. The tumor tends to destroy the surrounding bone but rarely gives rise to the more or less typical eye findings of the pituitary tumor, and moreover in its earlier stages it would not produce a ballooning of the sella turcica but would tend to confine its activities chiefly to destroying the dorsum sellae.

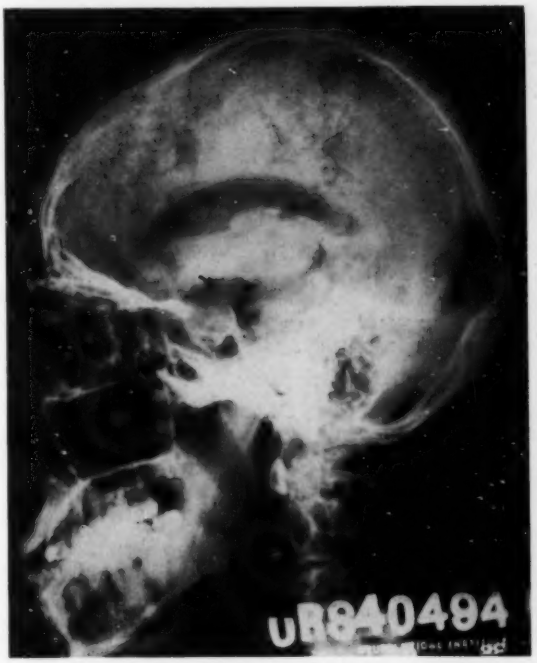

Fig. 13. Encephalogram showing a chromophobe pituitary adenoma which has extended above the sella turcica. Note the curved indentation of the anterior portion of the cisterna interpeduncularis and the small bubble of gas in the cisterna chiasmatis. The hypothalamic portion of the third ventricle is indented.

A carotid aneurysm may at times simulate a pituitary adenoma both clinically and roentgenologically. If the sella turcica is unilaterally atrophic and we find the optic foramen on the same side enlarged, and in addition see curvilinear streaks of calcification close to or above the sella turcica, an aneurysm is definitely indicated. But if all or any of these cardinal signs are missing we might have to employ encephalography or even arteriography, using thorotrast as the opaque medium. Even this may at times be confusing due to the possibility of the aneurysm becoming partly clotted and leaving only a relatively small lumen through its center.

An arterial angioma may at times prove to be a confusing factor, but fortunately

over 50 per cent of blood vessel anomalies calcify and so reveal their presence by parallel streaks of calcification in the vessel walls which are apt to be convoluted. Changes caused by such an anomaly in the sella turcica may simulate a pituitary adenoma by transmitted pulsating pressure, even from a considerable distance. The detecting of a bruit by auscultation would be diagnostic. In addition, an arterial angioma is usually accompanied by one or more large vessel channels in the vault. It would only be the small, deeply seated anomaly that might prove to be a confusing factor in a differential diagnosis.

Of the extremely rare forms of lesions which might confuse us in a diagnosis of pituitary tumors, might be mentioned the epidermoids, tuberculomas and gummas. In the case of the epidermoids and gummas unless the tumor involved the bone it might be impossible to make a definite differential diagnosis, but as the presence of such lesions is a remote possibility, we need not worry if one should occasionally be overlooked. The tuberculoma is rare but usually calcifies so that such a lesion could be recognized as extrasellar unless the pituitary body were actually involved. The history would play an important part in the diagnosis of a tuberculoma or a gumma. Gummas can occur in the presence of completely negative serological tests.

Not infrequently we may encounter a sella turcica which is "ballooned" in a manner very strongly suggesting the presence of an intrasellar adenoma, but there will be no symptoms at all suggestive of such a lesion. Such alterations in the sella turcica are often produced by tumors, usually gliomas, which may be remotely situated from the pituitary gland but have caused the changes in the sella turcica by transmitted pressure, as a rule through the ventricular system. The history of the case, together with the not unlikely finding of calcification in the tumor will draw our attention away from the hypophyseal region. It is often necessary in such cases to employ encephalography in order to be sure.

The treatment of pituitary tumors is rapidly becoming a non-surgical problem since such comparatively good results are being obtained by roentgen irradiation. Every case, however, should be given the benefit of a neurosurgical consultation because if the eyesight is in immediate danger or the tumor is so large as to raise the intracranial pressure, surgical interference should be seriously considered. Many workers have reported success with the radiation treatment of pituitary tumors, and a fairly large group of such cases have been treated at this clinic where they have been followed for considerable periods of time. This work has been reported by Dyke who has convincingly shown the good results obtained. However, a certain proportion of pituitary adenomas do not recede in size under irradiation, although the general symptoms may improve with no improvement of the eye fields. These tumors are evidently of the cystic type and constitute about one-fifth of those we see. After such a case has had an "irradiation test" of one or two series of treatments and no improvement is seen in the visual fields, it would be wise to consider surgical interference. The basophilic adenoma is evidently quite radioresistant, although intensive irradiation will occasionally produce a favorable result. Forms of treatment may vary considerably and the results will be quite comparable because most of us have come to realize that the "r" dosage by no means tells the story of what the biological reaction will be. The method with which I am most familiar consists in the use of a moderately high voltage, from 150,000 to 200,000, with filtration varying from 4 mm. of aluminum alone, to 0.5 mm. of copper plus 1 mm. of aluminum. The series consists of six to ten treatments given two or three a week, each treatment consisting of 200 to 250 r, measured in air, and applied equally over the two temporal regions and the frontal region usually through the ethmoid labyrinth. These series of treatments should be repeated at intervals of about a month or six weeks until two or three have been given;

CHART I

DIFFERENTIAL DIAGNOSIS OF TUMORS OF THE HYPOPHYSIS CEREBRI

Type of Lesion	Growth	Extrasellar Skull Changes	Changes in Sella Turcica		Evidences of Increased Pressure	Calcification	Vascular Changes	Shift of Pineal Body	Variations in Optic Canals	General Remarks
			Early	Late						
Adenoma Chromophobe	Slow	No definite change	Slight loss of calcium from cortex of posterior clinoids and dorsum	Ballooning and enlargement with atrophy which may be extensive	Very rare, 2 to 3 per cent	Very rare	None	Only if tumor becomes very large	Occasionally enlarged, usually unilateral	Usually occurs in young adults and frequently accompanied by primary optic atrophy with bitemporal hemianopia
Adenoma Chromophile	Slow	Acromegalic (adult). General enlargement (preadult)	May be no change or slight atrophy of posterior clinoids and dorsum sellae	Changes may be very slight; often not much enlargement or atrophy	Very rare	Extremely uncommon	None	Very uncommon; the tumor is not apt to be large	No changes expected with a true chromophile tumor	
Adenoma Basophile	Slow	None or a general irregular halisteresis giving a granular appearance	None; tumor usually very small	Often none or slight atrophy of dorsum sellae and floor	None	None	None	None	None	
Adenoma Mixed	Slow	May simulate either chromophobe or chromophile	This type of tumor has no characteristics as far as bone changes are concerned. If the tumor is obviously large and acromegalic changes are evident, the tumor is probably mixed because the adenoma producing acromegaly (chromophile) is usually small							
Adenocarcinoma	Usually rapid	None, unless metastases occur which would cause destructive lesions	Portions of the sella would appear dissolved—not merely atrophic	Complete dissolution of sella turcica and adjacent bone	None	None	None	Rare	May be present; not common	The rapidly malignant history and possible metastases will usually differentiate this type of tumor.
Craniotuberal epithelioma. Tuberal cyst	Usually slow; may lie dormant for years	May be general loss of bone calcium	None, or due to slight dorsal atrophy the sella seems shallow	May be none, or various grades of sellar destruction and enlargement	Often present	Very common; usually in the cyst or outlining its walls	None	Not uncommon	Rare	These are usually lesions of childhood, although not uncommon in adults below forty years of age. Usually accompanied by papilledema and/or primary optic atrophy.
Craniopharyngioma. Rathke pouch cyst		Usually indistinguishable from the tuberal cyst—calcification may be more intrasellar—and Fröhlich's syndrome is more apt to be a factor								

CHART II

LESIONS WHICH MAY SIMULATE THE ROENTGENOGRAPHIC FINDINGS OF PITUITARY TUMORS

Type of Lesion	Growth	Extrasellar Skull Changes	Changes in Sella Turcica		Evidences of Increased Pressure	Calcification	Vascular Changes	Shift of Pineal Body	Variations in Optic Canals	General Remarks
			Early	Late						
Meningioma (Suprasellar)	Slow	May be none or some bony hypertrophy of tuberculum sellae	Usually none	May be slight enlargement and general atrophy	Usually none	Very rare	None	Not usual	May be unilateral enlargement	Most prevalent in patients forty to fifty years of age. Often accompanied by bitemporal hemanopia
Glioma (Optic chiasm)	Slow	None	May be none or very slight atrophy of tip of dorsum sellae	Changes not apt to go beyond slight atrophy of dorsum sellae and floor	None	Very rare	None	Rare	Common; may be bilateral	Most frequently found in childhood. Patients usually exhibit primary optic atrophy with irregular field defects
Chordoma	Slow	Atrophy of clivus	Slight atrophy of dorsum sellae and posterior clinoids	Marked destruction of entire sella, usually without definite enlargement	Rare	Rare	None	Not uncommon	None	Rare tumors; might be difficult to differentiate from carcinoma or transitional cell epitheliomas, except that they are usually found in young patients
Aneurysm (carotid)	May be rapid	None	Slight atrophy of one posterior clinoid and side of dorsum	Considerable enlargement and unilateral atrophy	None	Common; curvilinear streaks above and to one side of sella	Only in arterial walls	Occasional	Enlargement of canal on side of aneurysm	Non-luetic lesion; may present a baffling diagnostic problem. Usually involves all structures in sheath of cavernous sinus
Granulomas Tuberculoma Gumma	Slow	Usually none	Usually none	May be slight atrophy of tip of dorsum	Usually none, unless lesion is subtentorial	May be seen in tuberculomas	None	Not usual	None	History must play an important part. Lesion can simulate all of the above mentioned lesions. Gummas have been found in the presence of negative serology
Extrasellar tumors in general	Varies	Varies; if present no confusion should exist	The same as for the pituitary adenomas		If present no confusion should exist	If present no confusion should exist	If present no confusion should exist	Common	Not common	The differentiation of extrasellar tumors varia calls for a familiarity with brain tumors in general (See charts)

CHART III

Intracranial Tumors	Percentage Incidence	Age Patients	Sites of Election	Growth Characteristics	Pressure Signs	Calcification	Bone Changes	Pineal Shift
Gliomas varia (See Glioma Chart)	45.0	All ages	Anywhere in brain	Rapid and slow	Usually present	13–14 per cent	Rare	Frequent
Meningiomas	15.0	Adult life, highest incidence about 40–50 years	Where arachnoidal granulations are most numerous—cribriform, sagittal sinus, sphenoid ridge, anterior half of cerebral convexities, petrous pyramids, foramina of base	Slow growing, displaces, does not invade brain	Occasionally present if tumor is large	Occasionally	Osteophytic changes usually predominant if tumor is in relation to bone—rarely osteolytic changes may be predominant	Frequent, if tumor is of any appreciable size
Acoustic neurinomas	8.7	Adult life, average age about 35 years	Eighth nerve usually near internal auditory meatus. Cerebellopontine angle	Slow growing	Atrophy of dorsum sellae may be noted	None	Destruction of petrous ridge and indirectly dorsum sellae	Not usual but depends on extent of tumor
Congenital	5.6							
1. Dermoids		Early life	Posterior fossa, but may occur anywhere	Slow—cystic; do not infiltrate	Present only if cyst is near cerebral fluid pathways	Frequent	Only those due to general increased pressure	May be present
2. Epidermoids		Early life	Over convexities or base (Pearly tumors)	Slow growing, do not infiltrate		Rare	Chiefly osteolytic, produces bone defects with dense margins	Rare
Blood vessel	2.0	Usually adult		Slow				May be present
1. Venous*			1. Parietal region		1. None	1. Frequent, and linear	1. None	
2. Arteriovenous*			2. Cerebral		2. May be present	2. in form	2. Pressure atrophy and deep vessel channels	
3. Hemangioblastomas			3. Cerebellar		3. Often present	3. None	3. Pressure atrophy	

* These are really anomalies and not true tumors.

Chart IV

Tumor	Percentage Incidence	Age of Patient	Sites of Election	Growth Characteristics	Pressure Signs	Calcification	Bone Changes	Pineal Shift
Metastatic	4.2							
1. Carcinoma		Adults	Anywhere in brain or bone; may be multiple	Rapid; infiltrating	Rare	None	Chiefly osteolytic with no evidence of bone regeneration	Rare
			Perivascular-meninges	Often slow; may be rapid	Rare	None	None with intracranial lesions	Rare
2. Sarcoma		Any age, usually beyond infancy						
		Adults	Brain or skull	Rather rapid	Depends on site of lesion (not common)	None	If lesion is in the skull bones osteolytic tendencies predominate	Rare
3. Hypernephroma								
		Adults	Bones of skull (all skeletal bones)	Fairly rapid	None	None	Small or medium sized areas of bone destruction, multiple and fairly well circumscribed—no bone production	Very rare
Granulomas	2.2							
1. Tuberculoma		Children (rarely adults)	Anywhere in brain	Slow	Depends on site of lesion	May be present	None except those of pressure	May be present
2. Syphiloma (Gumma)		Adults	Meninges or skull bones (usually multiple)	Slow	None	None	If in skull, the bone shows a defect without evidence of repair	May be present
Papillomas (of choroid)	0.6	Early childhood; less common in adults	Lateral ventricles roof of third and fourth ventricles	Slow	Usually present	May be present	Those of generalized increased intracranial pressure	Frequent
Osteoma	0.6	Usually adults	Ethmoidal region, orbito-ethmoidal, frontal sinuses, middle fossa, petrous pyramids	Slow	None	None	The tumor is composed of dense bone if a true osteoma, or not so dense if an osteochondroma	Rare

Chart V

Gliomas	Percentage Incidence	Age of Patients	Sites of Election	Growth Characteristics	Pressure Signs	Calcification	Bone Changes	Pineal Shift
Glioblastoma multiforme	30+	Adults	Cerebral hemispheres	Rapid, infiltrating	May be present	Often	Only those due to increased pressure	Frequent
Astrocytoma	40	Any age	Anywhere in brain (posterior fossa in children)	Slow; may be cystic	Frequent if in posterior fossa	Often in adults	Those of pressure only	Frequent
Medulloblastoma	10	Children	Cerebellum	Rapid; often invades meninges (radiosensitive)	Very common	Practically never	Those of pressure only	Not seen as a rule in children
Oligodendroglioma	4	Adults	Cerebrum	Very slow	Rare; may be slight sellar atrophy	Frequent	Chiefly confined to atrophy of dorsum sellae	May be present
Spongioblastoma (polare)	4	Children	Brain stem and optic tracts—associated with peripheral neurofibromatosis	Slow	Not common but may be noted	Rare	May show atrophy of walls of optic foramina and atrophy of sella turcica	Usually not seen
Ependymoma	0.6	Usually children or young adults	Along walls of ventricles—usually the fourth (spinal cord)	Slow	Usually present	Occasional	Those of generalized increased pressure	Usually not seen
Astroblastoma Pinealoma Ganglioneuroma Neuro-epithelioma	Very rare	With the possible exception of the pinealoma, it would be practically impossible to identify these tumors in the roentgenogram						

then it would be wise to wait a few months in order to be sure what the final results will be. In any event, one should hesitate to go beyond five of these series. The eye fields must be checked at intervals of about a month. The chromophile adenoma usually responds more rapidly to irradiation than does the chromophobe.

The treatment of the craniotuberal cyst and craniopharyngioma is moderately successful as far as delaying the refilling of the cyst is concerned after it has been evacuated surgically. Carpenter, Chamberlin and Frazier have reported on several such cases. These cysts are very prone to refill promptly after surgical drainage, and their complete removal is almost impossible, so that any procedure which slows or stops the refilling is a distinct asset to our methods of treatment. The modus operandi for treating these cystic tumors should be about the same as with the pituitary tumors except in the case of very young patients where the dosage might well be reduced slightly. Although in cases of this kind where there is practically nothing to be lost and everything to be gained it would be well to keep the dosage as high as possible. Nausea will occasionally be a factor to contend with, particularly in treating children, so that at times it might be advisable to apply smaller doses at each application, but the total dose for the series should be kept about the same.

SUMMARY

A short résumé has been given of the chief points of interest in a differential diagnosis of tumors of the hypophysis cerebri by means of the roentgen ray. Charts have been appended to aid in the differential diagnosis from most forms of intracranial tumors. The treatment of pituitary tumors has been very briefly discussed, and for those interested in a further pursuit of this entire subject of hypophyseal tumors a fairly extensive bibliography has been added.

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Vol. 40, No. 4

ENLARGED PARIETAL FORAMINA

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SMALL foramina in the parietal bones are regarded as normal, although they do not occur in all individuals; both parietal foramina are present in less than 50 per cent of persons, according to anatomists who have studied large series of skulls. One foramen occurs in about 25 per cent, while no foramen is present in approximately 25 per cent. A small percentage shows more than two. Normally the parietal foramina are 1 to 2 mm. in diameter; over 4 mm. may be regarded as abnormally large. In the cases of enlarged foramina reported, the size varies from 5 to 6 mm. in the longest diameter, to several centimeters. The enlarged foramina are of various shapes, sometimes round, more frequently oval, sometimes irregular. They usually lie close to the median line, and sometimes are separated only by a narrow bridge of bone.

The earliest descriptions of enlarged parietal foramina naturally relate only to anatomical specimens. Greig (1927) credits Lancisi with first describing an enlarged parietal foramen (unilateral) in 1707; Pamperl states that Lobstein in 1772 described a skull showing bilateral enlarged parietal foramina, but gave only few details of this specimen. The first clear and definite description was given by Turner in 1865. This is as follows:

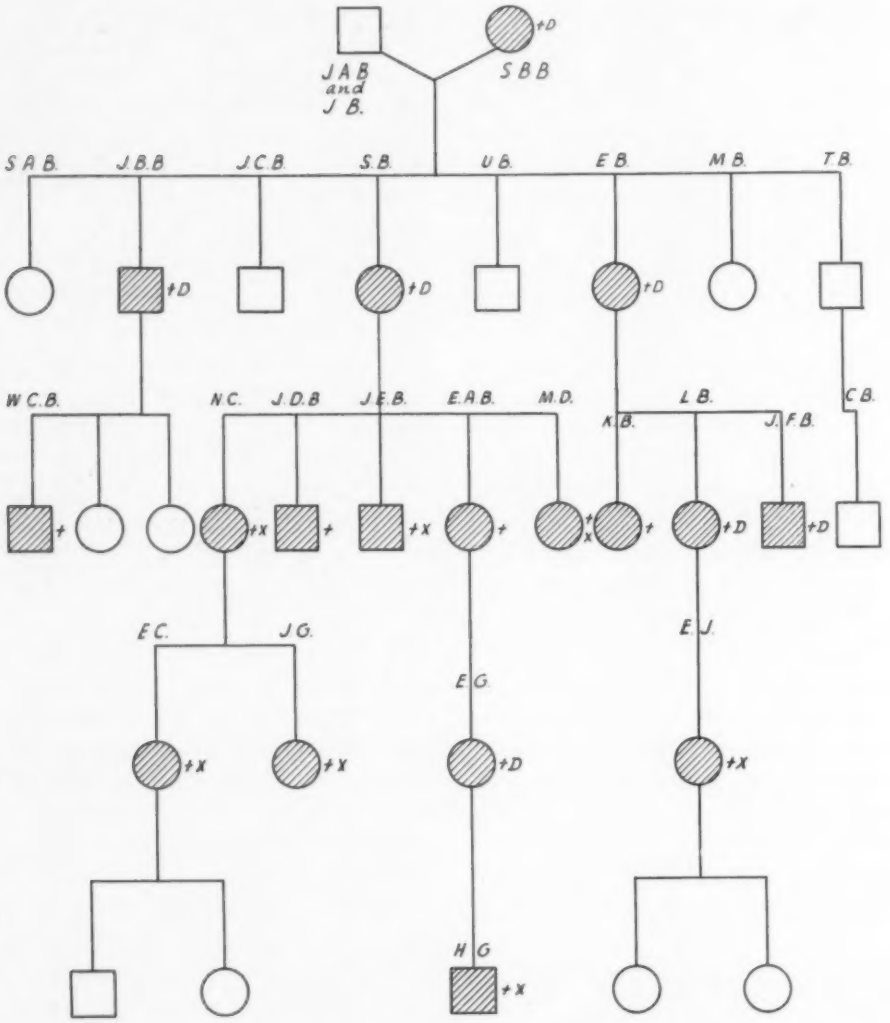
> At the commencement of the posterior slope of each parietal bone, an oval opening, possessing a rounded margin, was situated, the inner end of each of which was about half an inch from the middle line. The long axis of each opening was transverse, that on the right side measured 8/10ths of an inch, that on the left 6/10ths; the antero-posterior diameter of the right was at its widest part 6/10ths, while that of the left was only 4/10ths of an inch.

In 1919, Pamperl recorded a case of enlarged parietal foramina diagnosed during life by roentgenological examination, and collected 35 other cases from literature; of these 35 cases only 4 had been diagnosed during life, Pamperl's case making the fifth. Pamperl omitted 2 American reports of autopsy specimens showing bilateral enlarged parietal foramina, one by Piersol (1902) and one by Skillern (1914). He also omitted a case diagnosed during life reported by Greig in 1916, although including an earlier case of Greig's.

The first case to be diagnosed during life was the early case of Greig's reported in 1892. In this case, the diagnosis was made by palpation, and showed two "unossified" areas, one in each parietal bone, "close to its posterior superior angle." The patient, who was a British soldier in India, was fully aware of the presence of these "soft spots in his head," and at first claimed they were due to a fall from his horse a few years previously, but later admitted that they had been present from childhood. Firm pressure over these areas caused pain, dizziness and "flashes of light" before the eyes. The cases of di Gaspero and Hartmann (cited by Pamperl) were both diagnosed during life by roentgenological examination. Di Gaspero stated in 1911 that with the increasing use of the roentgen ray it is to be expected that more cases of this anomaly would be diagnosed during life. This prophecy has been well fulfilled in later years.

Since the date of Pamperl's article (1919) Boyd, Cave, Greig (1927), Stallworthy, and Stibbe have published descriptions of skulls showing enlarged parietal foramina, but there have been 11 cases reported that were diagnosed during life, and 7 reports of studies of families in which several members of the family have showed the defect. Of the 11 case reports, 3 also mention the examination of some other members of the family, although not a complete familial study. Thus Hässler (1936) reports a case of a child and roentgenological examination of the mother of the child, the mother's three brothers and her father; of these only the

FAMILY CHART



Explanation of Signs

\+ —presence of defect (enlarged parietal foramina).

D —deceased.

× —presence of defect proved by roentgen examination.

○ —female.

□ —male.

● *or* ▨ —definite information available.

○ *or* □ —no information obtainable.

mother showed a visible foramen in the right parietal bone. Marie reports a case of a boy thirteen years of age, and states that neither the parents nor his four brothers and sisters showed any similar cranial defect. Weill-Hallé and Weill report a case in an infant and state that the parents and another child showed no abnormality.

As early as 1895, the possibility of the familial occurrence of enlarged parietal foramina was suggested by Symmers, who reported the finding of this anomaly in the skull of a man dying at the age of forty. He states that: "On inquiry it was found that the father of this man had a similar abnormality of the skull." Greig's second case reported in 1916 occurred in the brother of the man in whom this anomaly was found in 1892. This second patient stated that he had known of the defect in his own skull and in that of his brother for many years, but that he was positive that neither of his parents nor any of his other brothers and sisters nor his own children had a similar defect. In 1922, an important study of the familial occurrence of enlarged parietal foramina was reported by Goldsmith. A study of five generations of this American family (the Catlin family) was made. The patient first examined who showed the anomaly

Fig. 1 N. C.; posteroanterior view.

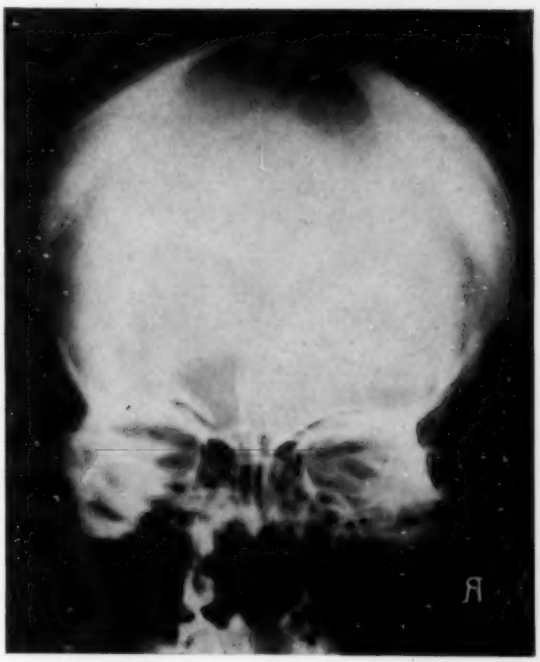


Fig. 2. E. C.; posteroanterior view.

was of the third generation; the "mark" was traced upward to the father and grandfather (first and second generation). The patient had two brothers and a sister who showed the anomaly, making 4 out of 16 members studied in this (the third) generation. It was noted that the sister was a twin, and her twin did not show this defect. Of 28 members of the fourth generation and 32 of the fifth generation studied, 10 had the defect. Goldsmith notes that: "The hereditary defect did not seem to fall in line with the usual laws of inheritance." In the same year (1922) Neurath reported a study of two German families. In the first family, a brother and sister and their mother showed very similar "defects" in the parietal bones; the father and a third child had entirely normal skulls. In the second family, mother and child showed the defects. In 1924, Cohn reported the occurrence of this anomaly in twins of the same sex (female) and in their mother; nothing further could be learned of the family; the mother's parents were dead; her older sister and the sister's child were both examined, but did not show the parietal defects. In 1932, Lelong and Bosquet reported a case

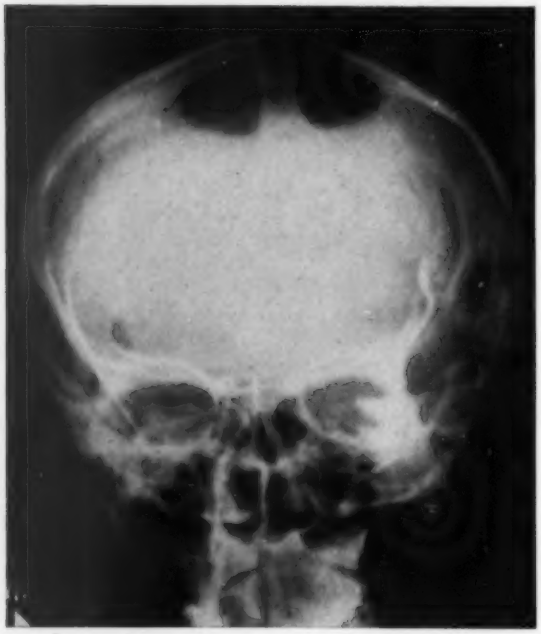


FIG. 3. E. J.; posteroanterior view.

in which the defects in the parietal bone were first found by palpation during a general examination of a boy aged five years; the roentgenogram confirmed the clinical findings. Subsequently the mother of this patient was examined roentgenologically, and showed exactly the same type of defect. She stated that her father had a similar abnormality, but he could not be examined. The patient's father and three other children in the family were entirely normal.

At the meeting of the American Roentgen Ray Society held in September, 1935, Pepper and Pendergrass of the University of Pennsylvania Hospital presented an important report on the hereditary occurrence of enlarged parietal foramina. The defect was found by palpation during the routine examination of a patient in the hospital. The patient stated that "these holes" had been present all his life, and that other members of his family showed the same anomaly. Roentgenograms were made and showed "a large rounded defect" in each parietal bone. Later the patient's mother, his sister, his son, and the sister's four children were examined roentgenologically. Of these, the patient's mother, his son, and one of his sister's children had large parietal foramina. The sister and one of her children had parietal foramina of smaller size, but definitely larger than normal. The patient's grandmother was not living but the family all stated positively that she had had "holes in her head." Thus of 9 members of a family in four generations, 5 had definitely enlarged parietal foramina, and 2 others bilateral foramina of smaller size, but larger than normal. Pepper and Pendergrass also had opportunity to study another family, a Negro family, in which the anomaly was first found in a young girl by roentgenologic examination. Later the mother and sister of this patient, two aunts and three cousins were examined. The patient's sister showed "a large merged defect" in the parietal bones, and one aunt had slightly enlarged parietal foramina. The family also "insists that the child's grandfather (maternal) had the same holes." The authors note "The promptness with which this family came to light once we knew of the anomaly suggests that the condition is not uncommon."

While the paper by Pepper and Pendergrass was presented in September, 1935, it was not published until January, 1936. In the meantime (December, 1935), Weber and Schwarz, in England, reported the study of a family, in which the first patient seen, a boy five years of age, had enlarged parietal foramina which could be felt and

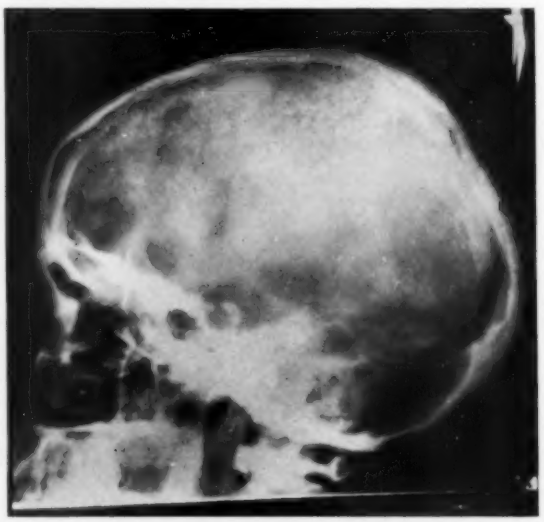


FIG. 4. E. J.; lateral view.

were also clearly demonstrated in the roentgenogram. This boy's mother had similar enlarged parietal foramina. Neither the father nor another child showed this anomaly. Of the mother's four sisters and two brothers, only one sister (a twin) showed the defect; the other twin, although of the same sex, did not show it. The mother's mother and (maternal) grandfather do not show the typical depressions in the head. The mother's father and (maternal) grandfather are not living, but did not show such depressions.

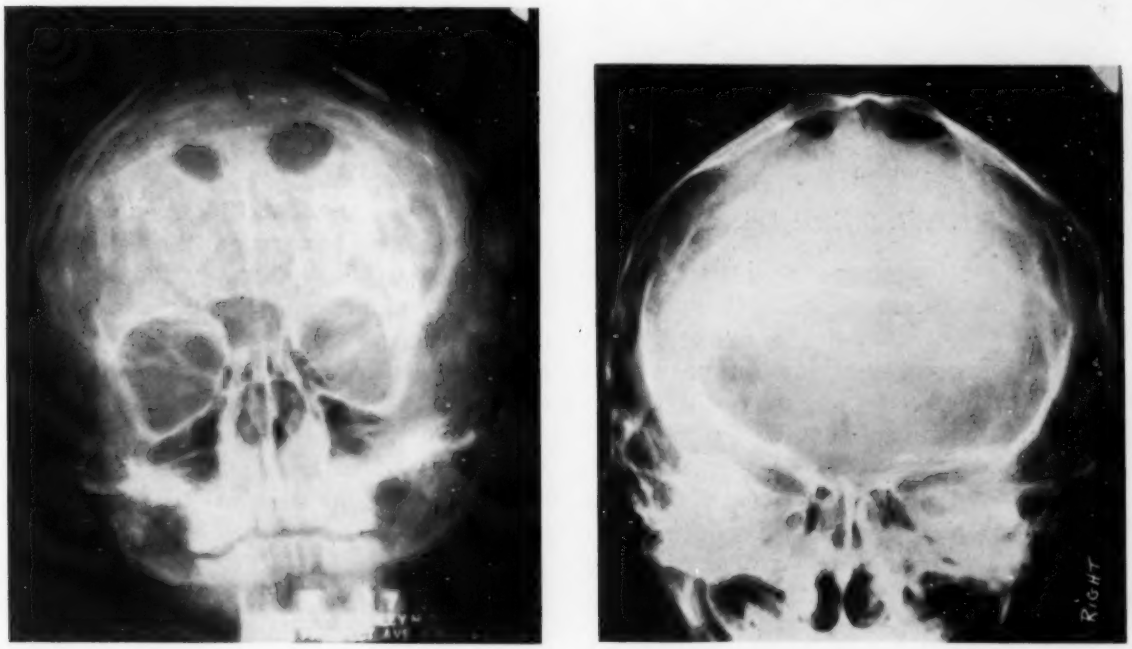


Fig. 5. H. D.; posteroanterior views.

In 1936, since the publication of the paper by Pepper and Pendergrass, two other studies of the familial occurrence of enlarged parietal foramina have been reported, one in England by Irvine and Taylor, and one in the United States by Alley. Irvine and Taylor saw 2 cases, both in children, in which the finding of the defects in the skull was "accidental." These two patients were not related, and an investigation of the family of each was made. In the first family clinical and roentgenological examinations were made of the father and mother and six of their children (including the patient), and also of the father's mother and brother and two of the latter's sons. Clinical examination alone was made of two other children, one of the father's nieces, and a nephew and a niece of the mother. Of the 18 persons examined, 5 showed the defect—the father and 4 of his children (including the patient). In the second family, the patient first examined was an only child. The father, his mother, sister and maternal aunt were examined; also the mother and her sister; only the patient's father showed the defect.

In Alley's family, the patient first seen was a boy who was given a roentgenological examination after an automobile accident. The enlarged parietal foramina were clearly shown, but could not be related in any way to the accident; it was some time before a correct diagnosis was made. Then the mother and 5 other children in the family were also examined roentgenologically. Of these, the mother and all but one of the children showed a defect similar to that of the patient. Alley's family was a Negro family and included a pair of twins, boy and girl, both of whom showed the defect.

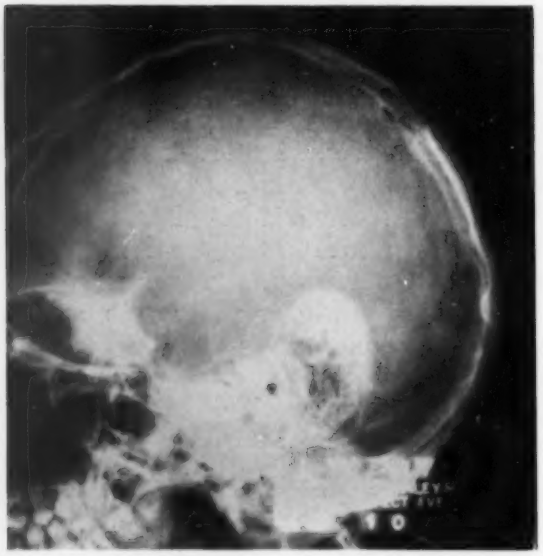


Fig. 6. H. D.; lateral view.

In most cases of enlarged parietal foramina, the defect has been found in the course of a general examination. Occasionally a special examination of the head has been made because of injury (as in Alley's case), or because of some neurological symptoms. Our first patient, N. C., a woman, aged sixty-three, was examined because of repeated attacks of headache with nausea and vomiting occurring at irregular intervals since early childhood. The headache was always frontal. These symptoms recently have been much relieved by the administration of ergotamine tartrate. But because of the possibility of an intracranial neoplasm a roentgen examination of the head was made. No signs of neoplasm or other intracranial lesion were found, but the roentgenogram showed two openings in the upper posterior portion of the parietal bones, near the median line on each side (see Fig. 1). In all our experience with roentgenological examination of the head, no exactly similar picture had been observed, but these openings resembled trephine openings or burr holes for ventriculography more closely than any other recognized condition. While the history of the patient was being more carefully investigated to determine whether a trephine operation or a ventriculography had ever been done, the article by Pepper and Pendergrass came to our attention, and we immediately recognized that our patient presented an example of the anomaly described in that article—enlarged parietal foramina. On questioning the patient, she stated that her mother (S. B.) had never had headaches, but had "soft places in her head." Further study of the family history showed that the patient's maternal grandmother (S. B. B.) had also shown the same defect. No further information was obtained in regard to this first generation, but in the second generation, in addition to the patient's mother, 2 of her 7 brothers and sisters are known to have shown the "soft spots." These persons were all deceased at the time this study was made. In the patient's generation (the third generation) definite information was obtained that enlarged parietal foramina were present in 9 out of 12 members, including the patient and her 4 brothers and sisters. This was confirmed by roentgen examination in the case of the patient and a brother and a sister. In the fourth generation there was reliable information that the enlarged parietal foramina were present in 4 persons; the

Fig. 7. M. D.; posteroanterior view.

patients 2 daughters, a niece (daughter of a sister showing the defect), and a second cousin (daughter of the patient's first cousin who showed the same defect). The niece was not living, but roentgen examination was made of the other 3 members of this generation, which showed the parietal defects. In the fifth generation information was available for only one person out of 5 known members of this generation; this was a grandnephew of the patient (son of the niece who showed the defect), in whom the roentgen examination showed typical enlargement of the parietal foramina (see family chart).

Enlarged parietal foramina occur in all races. Our family, as noted, was a Negro family; one of the families studied by Pepper and Pendergrass and Alley's family were also Negro families. The other cases diagnosed during life were in the white race. But in the anatomical specimens studied, this anomaly has been found in prehistoric races, Egyptian mummies, and various aboriginal races, as well as in civilized man. In 1875 Broca described enlarged parietal foramina in a Negro skull, which were not as large as those found in his other two specimens, but definitely larger than normal. A study of the family chart of our patient and of the family histories given by others leads us to agree with Goldsmith that the heredity of enlarged parietal foramina does "not seem to fall in line with the usual laws of inheritance."

Fig. 8. J. G.; posteroanterior view.

Fig. 9. J. T. B.; anteroposterior view. Roentgenograms of this case taken through the kindness of Dr. F. B. Mandeville, Memorial Hospital, Richmond Va. (The patient lived near Richmond, Va.)

In some cases of enlarged parietal foramina reported, the presence of other congenital defects or anomalies have also been noted; thus Greig states that the two brothers seen by him showed "a slight Mongolian cast of features" and microcephalism. In other cases there have been neurological symptoms such as headache or even epilepsy (Pamperl) associated with enlarged parietal foramina, but not apparently due to the defect. In the family that we have studied, besides the patients first seen, one of her daughters and one member of her own generation (a cousin) complained of headaches of the same type but not accompanied by vomiting. One of the patient's brothers was deaf and dumb. There seems to be no reason to consider that the headache in these cases, which was always frontal in type, was in any way due to the enlarged parietal foramina. As one member of the family—the patient's grand

Fig. 10. J. T. B.; lateral view.

nephew—had allergic eczema, hay fever and asthma, it seems to us much more likely that the headache noted in a few members of the family was of a migrainous and probably allergic type. In most cases, it is noted that persons showing enlarged parietal foramina are entirely normal in both physical and mental development. In a number of cases the patients, or in the case of children, their parents, are aware of the presence of "holes" or "soft spots" in the head, and do not regard them seriously. Pepper and Pendergrass report that their first patient was "greatly amused" by the interest shown and their "speculations as to the nature of the deformity."

Enlarged parietal foramina, therefore, appear to be of little clinical significance. Their chief interest to the roentgenologist lies in their correct interpretation so that they may be recognized and not confused with other conditions. Alley notes that he was unable to make a correct diagnosis in his first case, as he could not relate the defect in any way to possible trauma, although the patient had been in an automobile accident, or to any other pathological condition; and it was not until three years later that the true explanation was reached after the publication of the article by Pepper and Pendergrass. In our own case also, the roentgenological appearance of the parietal defect did not suggest any pathological condition, but rather trephine openings or burr holes for ventriculography. In a discussion of the paper by Pepper and Pendergrass, Sosman notes that he classed symmetrical defects in the parietal bones as trephine holes for ventriculography in a case in which there was no history of any such procedure, but was later convinced that these defects were enlarged parietal foramina. These defects might, however, be confused with some pathological conditions such as Hand-Schüller-Christian's disease, secondary neoplasms, traumatic defects, osteoporosis circumscripta, etc., but we believe that they are more likely to be confused with burr holes for ventriculography, unless very large or irregular in outline.

We would like, therefore, to call attention to certain differences between enlarged parietal foramina and burr holes after ventriculography, as seen in roentgenogram. The burr holes are absolutely symmetrical, of definite size and farther removed from the median line. Enlarged parietal foramina are often asymmetrical, varying in shape and size on the two sides, nearer the median line, often being separated by only a narrow bridge of bone, and frequently oval or irregular in shape rather than round. While their margins are smooth and usu-

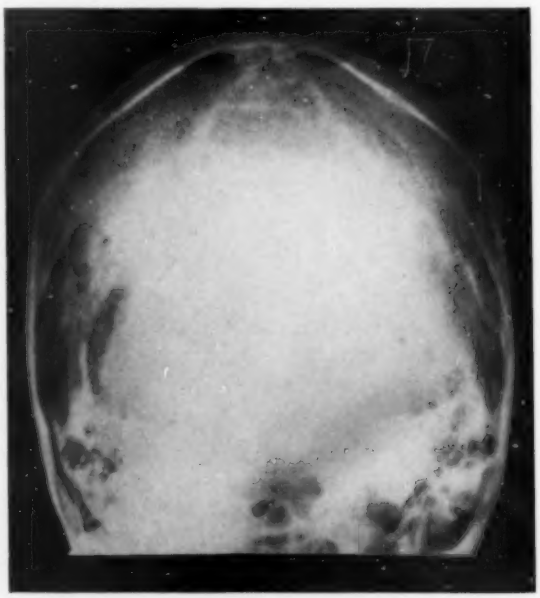


Fig. 11. J. T. B.; basal view.

ally well defined, in which they differ from many pathological lesions, the inner margins are usually less well defined than in trephine openings or burr holes. It is important that the roentgenologist should recognize this anomaly when he sees it, and whenever possible, make a study of its occurrence in the family of those patients in whom it is first detected.

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EPIPHYSEOLYSIS OR SEPARATION OF THE CAPITAL EPIPHYSIS OF THE FEMUR IN ADOLESCENCE*

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INTRODUCTION

ALTHOUGH definite progress has been made recently in the therapy of slipped femoral epiphysis, it is unpleasant to admit that the results of treatment have heretofore been disappointing, as we demonstrated in our study of the end-results of the treatment of over one hundred cases of this disease seen at the Hospital for Joint Diseases up to 1933.[6] During the past few years, however, there has been some modification of these methods due to newer concepts of the pathogenesis of the process. As a consequence thereof, the surgical attitude has been modified, so that there is now some unanimity of opinion regarding the treatment of some of the phases of the disease.

A review of the material seen in this institution during the past fifteen years convinces me that the most satisfactory results will be achieved in the early stages of this disease. It is for this reason probably that the treatment of more recent cases has been unquestionably better than in the patients who were treated five years ago. In the interim, we have learned to recognize the process in its early stages and to choose the most effective procedure.

Although the interpretation of the roentgenograms in the early cases is extremely simple, the roentgenologist too frequently fails to recognize the lesion. Unfortunately, this disease is infrequently seen in general hospitals and there is little opportunity to become familiar with its various phases. As a result, the difficulties of satisfactory treatment are immeasurably increased or else valuable time is lost and a simple condition is converted into a permanent deformity. It is apparent, therefore, that it is most important for the roentgenologist to familiarize himself with the disease, and its implications for its early recognition means its cure.

This study epitomizes the experience acquired from approximately 200 cases of slipped femoral epiphysis, and in this communication, it is my intention to review some of the roentgenographic features which characterize the lesion.

Our understanding of what occurs will be facilitated if we consider the normal adolescent hip and then its roentgenographic appearance in the various phases of slipping. It would be ideal for my purpose to utilize an adolescent hip obtained at autopsy but this I have unfortunately been unable to do. I shall have to confine myself therefore to a description of the normal hip for the fundamental considerations and utilize the roentgenograms of typical cases of slipped femoral epiphysis for illustration. Within certain limits, the stages of the deformity can be experimentally reproduced. This, Dr. Henry Milch and myself were able to do by utilizing the femur of a monkey loaned to him by Professor E. T. Engle of the Department of Anatomy, Columbia University College of Physicians and Surgeons. The roentgenograms obtained in this study were exhibited by us at the meeting of the American Academy of Orthopedic Surgeons in Cleveland in January, 1937.

DEVELOPMENT OF THE HIP JOINT

It is the proximal extremity of the femur which interests us in this study.[1,4,5] This segment is formed by three separate centers of ossification: one each for the head and trochanters. The epiphysis of the femoral head which begins to ossify during the second half of the first year is fairly well

* From the Department of Radiology, Hospital for Joint Diseases, New York. Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

demonstrated by the end of the first year. Its growth is extremely rapid so that by the third year, it surmounts entirely the femoral neck. After this period, its development is relatively slow until about the tenth year. At this time, a projecting "hump" or lip of the upper quadrant of the epiphysis projects slightly beyond the femoral neck. There is some discrepancy among authors regarding the period of complete ossification of the head to the neck, but it is variously given as occurring between the ages of fifteen and eighteen. In our experience, it is safe to assume that this union occurs at or about the sixteenth year. In its ultimate state, the capital epiphysis is symmetrically placed upon the supporting column of the neck.

The epiphyseal cartilage plate, which is roentgenologically referred to as the epiphyseal line, appears on the roentgenogram as an extremely broad band at or about the end of the first year. Although at first horizontally placed, it becomes progressively oblique as adolescence is approached. According to some authors, this change in the plane of the cartilage plate favors displacement of the epiphysis. As epiphyseal growth advances, there is reduction in the width of this band so that at or about the eleventh or twelfth year it appears as a reduplicated line between the epiphysis and femoral neck. For some time after complete ossification has occurred, this line may still be traced in the bone but it gradually fades out and disappears.

The lesser trochanter appears at approximately the ninth year and is united with the shaft at or about the sixteenth year. The greater trochanter appears at or about the fifth year and is completely united with the shaft at or about the sixteenth year.

The femoral neck is originally developed as an upward growth from the shaft. At birth, the angle of the neck to the shaft of the femur measures about 160 degrees, but it gradually decreases during the period of development so that, in the adult, it averages 125 degrees. Although the femoral neck forms an angle of 125 degrees in the vertical plane, it is important likewise to remember that it is inclined anteriorly to form an angle of approximately 15–35 degrees with the shaft. As adolescence is approached, the femoral neck becomes longer. It is important for the student to realize the significance of these facts since progressive anterior rotation of the femoral neck is now considered an important factor in the diagnosis and treatment of this disease.

The acetabular fossa is formed by the ischium, ilium and pubic bones and is fairly well demonstrated at birth. At this time, it consists of a cavity divided roughly by a Y-shaped incisura into an upper or iliac portion and a lower, ischial quadrant. The growth and development of this fossa are extremely rapid. Roentgenograms taken at or about the first year show a well-formed cavity containing an already well-developed femoral head. The growth of the upper quadrant appears to be more rapid than the lower half of the fossa so that, by the end of the second year, the acetabular shelf is sufficiently formed to prevent migration of the femoral head. The incisura which divided the acetabulum into halves rapidly ossifies so that at or about the thirteenth year it has completely disappeared. Complete ossification of the acetabulum therefore occurs at a time when the epiphyses of the femur are still visible although well advanced in their development.

THE ROENTGENOGRAM OF THE NORMAL HIP IN VARIOUS PROJECTIONS

The capital epiphysis in adolescence is well formed and hemispherical in shape. Its trabecular structure is usually well defined and of even texture indicating that "pressure is equally divided over the heavy surface of the sphere."[5] The base rests on the supporting column of the femoral neck from which it is separated by a narrow epiphyseal line. The upper quadrant of the head projects slightly beyond the upper limits of the neck. The epiphyseal line in actuality represents the radiolucent epiphyseal cartilage plate, its limiting barriers being formed by the contiguous surfaces of

the epiphysis and femoral neck. This line is clearly visible up to the age of fifteen to sixteen, while at the age of eighteen only a single linear density can be seen representing the point of junction of the femoral head and neck. While the plate surface of the capital epiphysis is fairly regular in contour and sharply defined, the opposing surface of the femoral neck is somewhat serrated. Thus it is difficult to determine just where the plate surface of the epiphysis ends and the neck begins, but this obscuration of the epiphyseal line is a normal finding. When the margins of the contiguous surfaces of the femoral neck and head are clearly defined, it is evidence of beginning slipping or detachment of the epiphysis and the explanation for this is simple. As the head and neck are freed, their plate surfaces separate and are thrown into relief by the tangentially directed rays. At adolescence, the obtuse angle which the neck forms with the shaft is approximately 125 degrees, as has already been indicated. The normal angle of anteversion* or antetorsion of the neck has been given as amounting to 15–35 degrees. The lower border of the femoral neck is longer and the cortex thicker than the upper border. In the normal hip, however, its upper border should never be convex. Such a change is usually an indication of coxa vara from whatever cause produced.

The greater trochanter invariably is well defined. Somewhat triangular in shape, its base rests on the outer aspect of the femur from which it is separated by a well-defined epiphyseal line. Occasionally, an accessory center of ossification appears at its apex and serves to increase the size of the prominence materially. Frequently, the base of the greater trochanter is likewise prolonged upward on the femoral neck for a limited distance. The lesser trochanter appears as a nipple-like projection on the inner surface of the shaft below the level of the greater trochanter and, at adolescence, its ossification is usually complete.

* The term "anteversion" employed in this communication does not imply a pathologic torsion of the femoral neck but merely the anterior rotation of the neck due to external rotation of the femoral shaft.

As the femur is brought into external rotation, certain typical changes occur. The lesser trochanter which is normally somewhat posteriorly placed is brought into relief and appears larger. With progressive external rotation, there comes a stage when this process faces directly forward, and in the anteroposterior projection it is completely obliterated by the dense shaft of the femur. Since the greater trochanter is an integral portion of the same segment of bone, external rotation results in a posterior migration of this prominence. With increasing external rotation, this trochanter gradually rotates backward until it is likewise obscured by the femoral neck. In order to understand the changing appearances of the femoral neck, it is important at this point to remember that the normal femoral neck joins the shaft at an angle of 125 degrees and that it likewise inclines forward at an angle of 15–35 degrees. As we rotate the femur externally, what do we actually accomplish? We are in effect increasing the anterior inclination of the neck. In the anteroposterior projection, therefore, the neck in a sense is coincidental with the central roentgen-ray beam and on the roentgenogram appears foreshortened. As we rotate the femur internally, the reverse phenomenon occurs. We apparently reduce the posterior inclination of the neck, and it is then brought broadside, so to speak, to the central beam. There occurs therefore an apparent increase in the length of the femoral neck.

The lateral projection is the position of choice in the early demonstration of epiphyseolysis, for by it the entire neck of the femur is visualized. The capital femoral epiphysis is likewise clearly seen but its projecting "hump" is not so characteristic as on the plates taken in the usual anteroposterior projection. The serration of the epiphyseal line appears to be reduced. In this view, the greater trochanter appears to be superiorly placed but is obscured by the neck and the intertrochanteric region. The lesser trochanter placed somewhat inferiorly is clearly demonstrated.

One quickly determines the position of the femoral shaft by the appearance of the trochanters and length of the neck. When the lesser trochanter is unusually prominent and the greater trochanter obscured, the femur is in external rotation. But if the greater trochanter is well visualized and the lesser trochanter obscured, the femur is in internal rotation. In extreme external and internal rotation, however, both trochanters are obscured, but the clue is furnished by the appearance of the femoral neck. If the neck is foreshortened, the femur is in external rotation but if it is of normal length or apparently increased, the femur is in internal rotation. This relationship is obvious in fractures of the neck of the femur.

Whatever the degree of rotation of the femoral shaft in the normal hip, the capital epiphysis remains of the same height and the appearance of its projecting "hump" is not materially altered. In extreme external rotation, however, the margins of the femoral head may be projected through the neck and appear as a semilunar density. This circular density is not to be confused with a somewhat similar density produced by the rotated femoral neck in epiphyseolysis.

ETIOLOGY

Key's[2] contribution on epiphyseolysis contains an excellent summary of the theories regarding this disease, and the subject matter for this section was obtained from that publication.

By many of its original investigators, epiphyseal coxa vara was considered a form of adolescent rickets and this conviction was fostered somewhat by the reports of the examinations of gross specimens. Although rejected by some, still later investigators inclined to this theory but further modified it to include all diseases capable of producing an osteomalacia. It is probable that this idea had its genesis in the World War because of observations made on undernourished patients. For it to be acceptable, however, it would be necessary to believe that either rickets or osteomalacia could be localized in one or both hips, but would still leave the rest of the skeleton intact. In the typical instances of these diseases with which we are familiar, no such deformity occurs.

It was suggested by some that the disease was a form of juvenile arthritis deformans and consequently no operations were performed to correct the deformity because of the belief that the bones were the seat of a trophic disturbance. This hypothesis is likewise difficult to accept. As I shall indicate later, the cases treated in the early stages of the disease heal without deformity. It is moreover the feeling of those who are familiar with this problem that the changes which occur in the femoral head are due solely to its detachment from the neck and are of a similar order to those observed in subcapital fractures of the femur. Roentgenologically, the articular surfaces of the femoral head and of the acetabulum do not participate in the process. It is my belief that the arthritic changes which may occur are purely secondary in nature or may follow the trauma incidental to some forms of treatment.

Frangenheim (quoted by Key[2]) found no evidence of rickets but believed that there existed some abnormality in the epiphyseal cartilage plate in the nature of a chondrodystrophy. The explanation of the etiology of slipped femoral epiphysis under this premise, therefore, is that the epiphysis slips on an already diseased epiphyseal plate. This theory or its modification is currently held by many orthopedists. That it has no basis histologically is the opinion of Sutro.[7]

No one who has studied this problem has failed to be impressed by the frequency with which epiphyseolysis occurs in individuals of the Froehlich type. These patients are usually fat or obese children of a eunuchoid habitus. It is for this reason that the disease is considered by some an endocrinopathy, and the gonads, thyroid and pituitary glands implicated. However, corroborative information is lacking. The cases studied by me have no suggestive changes

in the basal metabolism, blood chemistry or sella turcica. Furthermore, this theory fails to explain the occurrence of this disease in children who do not present this classical picture. Yet, despite the absence of positive proof, it is hard to free ourselves from the conviction that there is some causal relationship.

The static theory assumes that the growing femoral neck is deformed by the superimposed or superincumbent weight of the body and for that reason it is considered in the nature of an occupational disease to be encountered or expected in those individuals whose work requires prolonged standing such as laborers and farmers. To prove this theory, its advocates quote cases which occurred in individuals of the farming or laboring classes. The Hospital for Joint Diseases derives its clinic patients almost exclusively from the urban population and practically all of its cases of epiphyseal coxa vara occurred in school children. It would be somewhat tedious and unprofitable to examine in detail all of the modifications of this concept. Doubtless the superimposed body weight, when disproportionate to the tensile strength of the femoral neck, would be a contributing factor. The pattern may be laid down in those individuals in whom there is a strong possibility of an endocrine disorder.

The rôle which trauma plays in this process is extremely difficult to determine. The histories of juvenile clinic patients are frequently unreliable, particularly when we attempt to separate what appears to be a significant injury from the casual blows sustained in play. That trauma of sufficient intensity may produce an acute separation of the epiphysis is too obvious to debate here. The question which arises, however, is whether the separation of the epiphysis is facilitated by a pre-existing disease of the epiphyseal plate. Judging from the roentgenograms of the epiphyseal lines of the cases which I have observed, there is no abnormality apparent and this impression is further corroborated by the studies of the histopathology of this disease. Theories regarding the effect of repeated small traumata are extremely speculative and add nothing of value. Key has suggested that the periosteal fibers which hold the epiphysis in place atrophy at or about adolescence and, as a result, a point of weakness is established at the epiphyseal line which facilitates the migration of the femoral head on the application of force. This theory is accepted by many orthopedists.

PATHOLOGY AND PATHOGENESIS*

It is only in the last few decades that the condition of slipped femoral capital epiphysis in adolescents has come to be clearly distinguished from many other conditions affecting the upper end of the femur and likewise resulting in coxa vara. This advance has been made mainly through the roentgenographic study of numerous cases of hip disease, which has permitted the recognition of slipped epiphysis in its early stages (that is, at a time when it is easily distinguishable from other conditions), and also made it possible to trace its progress and end stages. Unfortunately, our knowledge of the pathology (and pathogenesis) of the condition has lagged far behind our roentgenographic knowledge, primarily because suitable material has usually not been available for pathologic study. Indeed, even in special institutions, most of the material available has consisted of fragments of bone removed at operation in regard to which it is often difficult for the pathologist to orient himself. In view of this situation it is understandable that confused and sometimes erroneous ideas of the pathology of the condition have arisen.

In a few instances of slipping of the capital epiphyses in adolescents, adequate material consisting of the femoral head and adjacent part of the neck have been available to us for pathologic examination. Serial sections of such material have shown that in contrast to what happens in Perthes' disease, the capital epiphysis itself is not primarily altered. On the other hand,

* Contributed by Dr. Henry L. Jaffe, Director of the Pathologic Laboratories, Hospital for Joint Diseases.

the epiphyseal cartilage plate shows marked aberrations from the normal. Specifically, if the plate is followed through the serial sections, it will be found buckled in some places, reduplicated in some, and in other sections quite fragmented and discontinuous. Furthermore, bits of epiphyseal cartilage plate, often surrounded by sclerotic bone, may be found in the capital epiphysis and even in the femoral neck, at some distance from the normal plate line. Indeed, in some of the sections the plate looks as though it had been spattered about by some disruptive force (Fig. 1). The slipped epiphysis is usually found firmly united to the neck but in a position of malalignment. The articular cartilage over the head is not necessarily much altered at first. Frank necrosis of the osseous trabeculae and the intertrabecular marrow is nowhere apparent. Near the disrupted plate and between the fragments of it, both toward the head and toward the neck of the affected femur, one finds areas of increased vascularization, fibrous tissue, and newly formed bone.

There seem to be several factors (which Sutro working in my laboratory points out) which normally combine to prevent slipping. One of these is a favorable tilt of the epiphysis in relation to the neck. Another is the support which the head receives from the inferior buttress of the neck. A third, and probably the most important, is the anchorage of the head in the neck by the collagenous fibers linking the periosteum of the neck to the epiphyseal cartilage plate. Abnormal weight against the head and neck may weaken or destroy any or all of these defenses and thus initiate slipping of the epiphysis.

The mechanism of the actual slipping and of the aforementioned disintegration of the epiphyseal plate may hence be conceived somewhat as follows: In consequence of abnormal functional stress, bunches of the fibers linking the periosteum of the neck to the plate, may tear at various points. Though there is as yet no actual separation of the epiphysis, the attachments of the latter are already weakened and slipping soon ensues. Additional functional trauma then seems to sever the periosteal fibers completely. Subsequently, there are various additional changes, such as fracture of the atrophic buttress of the inferior cortex of the neck, or compression of that projection. Finally, the activity of the muscles about the hip joint tends to separate the epiphysis completely from the neck. Recurrent traumatic wear and tear directed against the epiphyseal cartilage plate (which remains attached to the head) accounts for the disruption and disintegration which the plate undergoes.

Fig. 1

In the course of time, the local evidence of slipped epiphysis becomes increasingly vague and the pathologic picture ultimately presented by the affected joint is likely to be that of a hypertrophic arthritis particularly pronounced in the articular end of the

femur. Indeed, it is frequently only by looking carefully into the history of the case that the arthritis which has ensued can still be connected etiologically with the slipping of the epiphysis and hence recognized as a secondary hypertrophic arthritis.

SYMPTOMATOLOGY

The clinical picture varies somewhat depending upon the degree of slipping of the femoral head. There is usually a history of pain which may occur after some unusual activity, but it may be absent, slight or severe in character. Pain may be localized in the involved hip or else referred to the thigh, knee, and at times to the foot. Except in the acute traumatic cases which are essentially fractures, pain is rarely severe and is subject to remissions. At times there is a history of recurrent episodes of pain of increasing severity until disability results. Symptomatic relief is obtained by rest in bed or immobilization. Even where pain is absent, there is usually a limp which may be noted first by parents or friends. The limp persists and is associated with some limitation of motion which is most marked in the acute traumatic cases.

On physical examination, one finds that the patient walks with a limp, with a pelvic tilt to the unaffected side. The involved extremity is usually shorter. Motion of the involved hip is restricted. The thigh is held is slight flexion. Adduction may be slightly limited but abduction is distinctly restricted. External rotation is free but internal rotation is distinctly reduced. In acute traumatic separation, as we have already indicated, the symptoms and signs are identical with those of fracture of the neck of the femur.

ROENTGENOGRAPHIC CHANGES IN SLIPPED FEMORAL EPIPHYSIS

For purposes of roentgenographic description and study, I have arbitrarily divided the lesion into the following types:

1. Slight slipping
2. Marked slipping
   (a) Acute
   (b) Chronic
3. Old cases

1. *Slight Slipping.* In the literature, there is constant reference to the term "preslipping stage," by which is meant an extremely early phase of the lesion when the clinical symptoms are suggestive and the roentgenograms supposedly negative. It is inaccurate to describe such a stage of the disease since it does not exist and the term should therefore be abandoned. When clinical symptoms are suspicious, careful roentgenograms—which must include a lateral of the hip joint—will show some alteration in the epiphyseal line, the femoral neck or the head. I have had occasion to review many of the plates of patients referred to the hospital for treatment in the so-called preslipping stage and, almost invariably, the original films showed the earliest phases of the disease which had either been overlooked or were unrecognized. It is obvious that the recognition of the lesion at this stage is of inestimable importance to the orthopedist since the prompt application of immobilizing devices limits migration of the femoral head and subsequent deformity.

The earliest stage of slipping can frequently be detected by the loss of the "hump" formed by the small projecting lip of the epiphysis which normally extends slightly beyond the superior border of the femoral neck. It may be the only roentgenographic evidence of the disease and it indicates that the epiphysis has become detached and has begun to slip. The lower pole of the femoral head may project below the lower border of the neck in the form of a beak or small process.

I have failed to note in this stage of the disease the osteoporosis of the capital epiphysis which has been referred to by some. When osteoporosis occurs, it is seen more characteristically in the advanced nontraumatic cases and in those following surgical intervention. I have noted a slight increase in the density of the base of the capital epiphysis which I believe indicates that its position has already been altered by internal rotation. The change in the axis of the epiphysis brings its plate surface into an anteroposterior plane so that it is seen

in profile. In taking the usual roentgenograms, the rays are projected through the thickest part of the epiphysis and produce an appearance suggestive of sclerosis, although no such change actually occurs. The apparent increase in the size of the head is due solely to its rotation on a vertical axis. The epiphysis remains within the acetabulum.

In some cases, the earliest evidences of disease are the alterations which occur at or near the epiphyseal line. Osteoporosis or resorption appears as a transverse band parallel to the epiphyseal line or else patchy, confluent, roughly circular zones are seen which extend into the neck for a distance of approximately one-quarter to three-eighths of an inch. I have observed

Fig. 2

these changes in bilateral cases on several occasions and was able to state correctly that slipping of the epiphysis was taking place. The significance of this observation still seems to be ignored by some clinicians, but a study of the cases collected in this institution to date has convinced me of the importance and reliability of this sign.

The third sign which is present is an increase in the width of the epiphyseal line. As the head and neck separate, the line of cleavage first occurs anteriorly and as a result a V-shaped hiatus exists between them. It is this gap—base forward—which is roentgenographically demonstrated as an increase in the width of the epiphyseal line (Fig. 2).

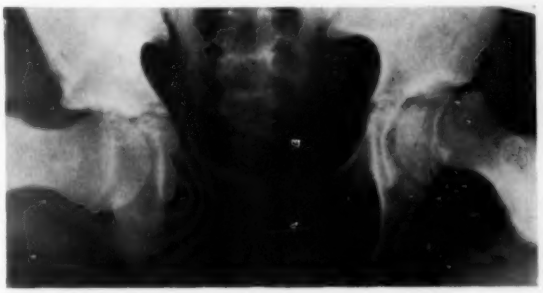

Fig. 3

In the extremely early cases, there is no perceptible alteration in the configuration of the femoral neck. The upper border of the neck adjacent to the epiphyseal line at this stage is simply freed from its attachment to the epiphysis and is noted as an irregular blunt projection. The femoral neck, however, is pulled outward and somewhat upward, as it is in fractures of the neck of the femur (Fig. 3). It is important for therapeutic purposes to establish this relationship unequivocally as the successful correction of the dislocation necessitates realignment of the femoral neck by internal rotation of the femur.

2. *Marked Slipping.* Clinically these cases may be divided into an acute or chronic type. In the acute type, there is usually a history of severe trauma with associated clinical symptoms of a fracture. In the chronic cases, there may or may not be a distinct history of trauma or else one of repeated mild injuries which may not be sufficiently severe to incapacitate. In any case, an injury may completely detach the femoral head and precipitate acute symptoms. It is often difficult or impossible to judge whether a case belongs to the acute

or the chronic type, as the histories of clinic patients are notoriously unreliable, and many children suffer repeated falls without epiphyseal displacement before their final injury.

The roentgenograms in this group show a fairly typical picture. The amount of displacement of the femoral head will of course vary with the chronicity of the process or else with the severity of the injury in

Fig. 4

the acute traumatic cases. The femoral head may be displaced downward a distance of one or one and one-half inches or may be completely separated from the femoral neck and lie free in the acetabular fossa. Depending therefore on the degree of displacement, the appearance of the head varies. As the femoral epiphysis is detached it rotates so that its articular surface faces downward, inward and backward. With rotation, its base or plate surface faces forward and since the plate surface is circular in outline, its projection on the film will be an ellipse or circle, depending upon the degree of rotation of the femoral head. In moderate slipping, it is usually seen as an ellipse, and in the cases of acute traumatic separation with complete rotation of the head, the plate surface faces anteriorly and is seen as a circle. It is astonishing how much separation may exist and be unsuspected on the film taken in the usual anteroposterior projection. There occurs, moreover, an apparent reduction in the height of the epiphysis depending upon the degree of displacement of the femoral head. The greater the displacement, the shorter the capital epiphysis. The epiphysis remains within the acetabulum although on a posterior plane to the neck, so that the head and neck form an angle whose apex is forward (Fig. 4).

As Milch[3] has indicated, the dynamics of the lesion may reside in a progressive anterior rotation of the femoral neck, and he correctly stresses that this rotation precedes and may exist even with correction of the varus deformity. The anteversion in this stage of the disease may be best demonstrated on the lateral views of the hip. In the films taken in the anteroposterior projection, its existence may be suspected by the appearance of a crescentic line of density over the femoral neck. Since the femoral neck is tubular in shape, anteversion brings into profile its limiting borders. Where a marked anteversion exists, the neck may face completely forward. In the phase of the disease which we are here discussing, the posterior border of the femoral neck is in contact with the plate surface of the capital epiphysis but at a point remote from its original point of attachment. Several crescentic densities are seen and their true significance may be appreciated only on stereoscopic vision (Fig. 5). As we trace these densities from without in, the outermost line represents the anterior rim of the femoral neck which has rotated forward, a second and somewhat indistinct line represents the posterior rim of the epiphyseal plate surface of the femoral head whose shadow is projected behind the neck. The third density is easily identified as the anterior rim of the epiphyseal plate surface of

the femoral head which has been rotated internally. These multiple crescentic densities are noted particularly in the inadequately treated cases. With anterior rotation, there is of course external rotation of the extremity and eversion of the foot.

3. *Old Cases.* The old cases represent essentially the end-results of pre-existing slipping of the capital epiphysis and in many instances are identical with those seen in united fractures of the neck of the femur. The idiopathic and traumatic cases cannot be differentiated. Under the circumstances, therefore, the roentgenogram presents a variable picture, depending upon the extent of the original slipping or upon the method of treatment employed. As a general rule, the disease is self limited and union invariably occurs.

In many instances of slipped femoral epiphysis where treatment was instituted, it may be impossible to recognize that this condition has ever existed. In others, and particularly in the untreated cases, the permanent change in the alignment of the head and neck may be readily recognized. In such instances, union occurs with the fragments in malposition. The lower border of the femoral head projects below the neck as a small beak-like process. Its width varies in individual cases. It may be crescentic or else mushroomed, depending upon the degree of the original slipping (Fig. 6). In long-standing cases, extreme eburnation of the articular surface of the epiphysis exists with the formation of extremely large osteophytes. Although we consider it almost axiomatic that most cases ultimately develop an arthritis, the severity of this process in old cases frequently masks the original condition.

Fig. 6

Fig. 5

The femoral neck may be foreshortened or elongated. Usually it appears to be foreshortened due to anterior rotation and to the fixed attitude of external rotation of the extremity. In the treated cases, the restoration of the normal length of the femoral neck is one indication of the success of the maneuver. In long-standing

cases, the upper border of the femoral neck is convex, whereas its lower border is concave and somewhat thickened. Occasionally, the thickening of the neck resembles that seen in Perthes' disease from which differentiation may be extremely difficult. In the cases of extreme slipping, the mesial portion of the neck may be rounded off and articulate directly with the acetabulum. Coxa vara deformity is almost invariable.

Fig. 7

The changes in the acetabulum are the obvious manifestations of the altered stresses and strains at the hip joint. Although the acetabulum is not a primary factor in the disease, the existence of the process in the femur serves as a chronic irritant which initiates an osteoarthritis and results in fixation of the hip.

The Roentgenogram of the Abnormal Hip in Various Projections

We can best appreciate what occurs in epiphyseolysis by studying a typical case. Figure 2 is the roentgenogram of a patient who was admitted to the hospital because of pain and a limp. On examination of the plate, it was noted that there was a distinct increase in the width of the epiphyseal line with a disappearance of the projecting "hump" of the epiphysis. Although this phase of the process might erroneously be termed the preslipping stage, the lateral roentgenogram showed a fairly marked detachment of the femoral head and anterior rotation of the neck (Fig. 3). One week later, slipping occurred and the roentgenogram showed a typical coxa vara deformity (Fig. 4). Although correction was attempted, the roentgenograms still showed subcapital densities. It was evident from these films that the anteversion antedated the coxa vara deformity and that this rotation of the femoral neck was in some way associated with these densities. After treatment and following union of the capital epiphysis to the femoral neck, the hip was again examined in the anteroposterior plane but this time roentgenograms were taken in external and internal rotation.

In external rotation (Fig. 7), there was a moderate diminution of the length of the femoral neck similar to that which occurs in normal cases. The capital epiphysis, however, appeared to be normally positioned. Since the epiphysis moved concurrently with the excursions of the femur, it was obvious that it was united to the neck. With progressive external rotation, aggravation of the deformity was to be expected. This paradoxical situation was extremely confusing until an explanation suggested itself. Since the femoral neck was in contact with the anterosuperior quadrant of the epiphysis, it was evident that, as the femur was brought into external rotation, the capital epiphysis was rotated upward and forward. If, therefore, external rotation was continued, a stage would be reached when complete derotation of the epiphysis could be accomplished and it would then apparently resume its habitual position in the acetabulum. The importance of this observation cannot be overstated. Since the capital epiphysis frequently unites with a residual rotation of

the femoral neck, and fixed position of external rotation of the femur may in the usual anteroposterior roentgenogram show a capital epiphysis which is apparently well aligned.

In the normal hip joint, internal and external rotation do not materially affect the size of the femoral head. In the cases cited, as the femur was rotated inward (Fig. 8), its capital epiphysis became smaller and somewhat crescent shaped. The femoral neck was increased slightly in length. It has already been seen from what has preceded that the rotation of the epiphysis is downward, backward and inward and that the anteriorly rotated femoral neck is in contact or fused with the anterosuperior quadrant of the epiphysis. In this case, as the femur was internally rotated, the femoral neck aggravated the rotation of the capital epiphysis and its vertical diameter was therefore materially reduced. Furthermore the posterior rim of the epiphysis was forced backward and on the roentgenogram was seen to be projected behind the femoral neck. Additional crescentic densities were noted over the femoral neck and a study of the identity of these shadows formed the thesis of Milch's contribution and the basis for our experiments.

Fig. 8

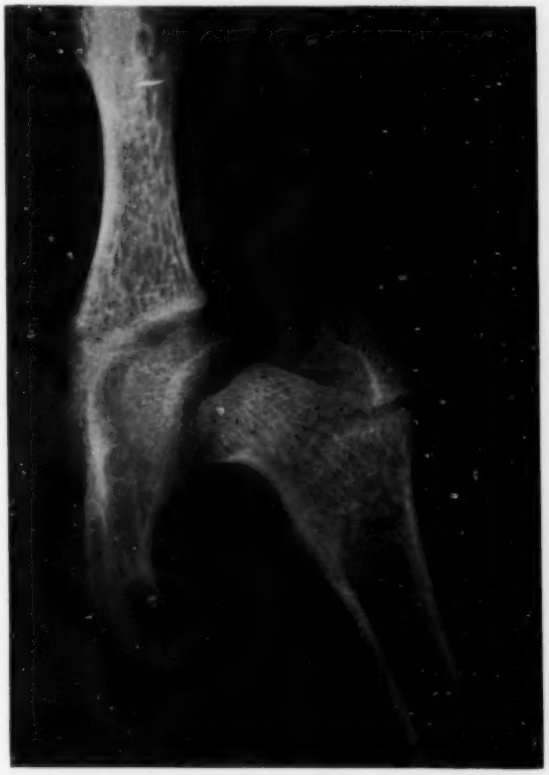

Fig. 9

The Roentgenograms of the Hip of a Monkey in Various Projections

In order to clarify in my mind the significance of the various roentgenographic appearances during the different phases of the disease, I attempted to reproduce the deformity at will. For this purpose, a femur of a monkey was utilized, although I realized the limitations imposed upon me by the very nature of the specimen. But the roentgenograms were instructive and clarified considerably the meaning of the densities and shadows which had heretofore puzzled me. Limitations of space preclude the possibility of including all the films made in this study, but pertinent examples will be illustrated.

The hip joint of a normal monkey was roentgenographed and the anatomical land-

Fig. 10

marks established. The roentgenogram duplicated closely those seen in the normal human adolescent hip.

The capital epiphysis was then detached in an effort to simulate the changes which occur in early slipping. Figure 9 shows the gap which exists between the capital epiphysis and femoral neck. A roentgenogram taken with the femur in internal rotation (Fig. 10) shows the migration of the femoral head. Note the reduction in the vertical height and internal rotation of the epiphysis. The posterior rim of its plate surface can be seen projected through the femoral neck.

The shaft of the femur was then externally rotated about 45 degrees (Fig. 11). In this position, the femoral head is seen to be rotated inward so that the plate surface presents anteriorly. The vertical height of the epiphysis is distinctly reduced and its posterior rim can be visualized through the neck. The femoral neck, as in the human, is on a plane anterior to the head and is likewise rotated outward. This film duplicates closely the roentgenograms of the cases of moderately advanced epiphyseolysis.

An additional plate of the hip was taken but this time the femur was rotated outward and abducted (Fig. 12). The capital epiphysis was completely detached. Note the crescentic density outlining the circumference of the femoral neck. This subcapital shadow is noted in most cases of moderately advanced and in all cases of advanced epiphyseal slipping, and must not be confused with the margins of the plate surface of the capital epiphysis. The femur was next rotated outward about 60 degrees and a steel needle inserted into the femoral neck parallel to its long axis (Fig. 13). It will be seen that the femoral head is within the acetabulum and that its height is not materially reduced. The femoral neck is rotated anteriorly so that its

Fig. 11

entire circumference now becomes visible. This film duplicates the situation which exists in acute epiphyseal separation.

As this problem was studied, it was apparent that the greatest mobility existed in the femoral shaft and that the excursion of the femoral epiphysis was somewhat limited as it remained in the acetabulum even in the advanced cases. Furthermore, it was observed that as the shaft was rotated progressively outward, the roentgenogram showed an enlargement of the subcapital density. Beginning as a small ellipse, it gradually increased in diameter so that when the femur was in complete external rotation, it appeared as a circular shadow resembling that seen in the human. The femur was then exarticulated (Fig. 14). It was now evident that the subcapital densities noted in the roentgenogram were in fact produced by the limiting borders of the femoral neck. Wires were closely wound about the borders of the plate surface of the capital epiphysis and the contiguous segment of the femoral neck. In the neutral position, these wires appeared as parallel bands, indicating the normal alignment of the capital epiphysis and neck. The roentgenogram taken with the femur in external rotation showed the anterior rotation of the neck so that practically its entire circumference became visible (Fig. 15).

Fig. 13

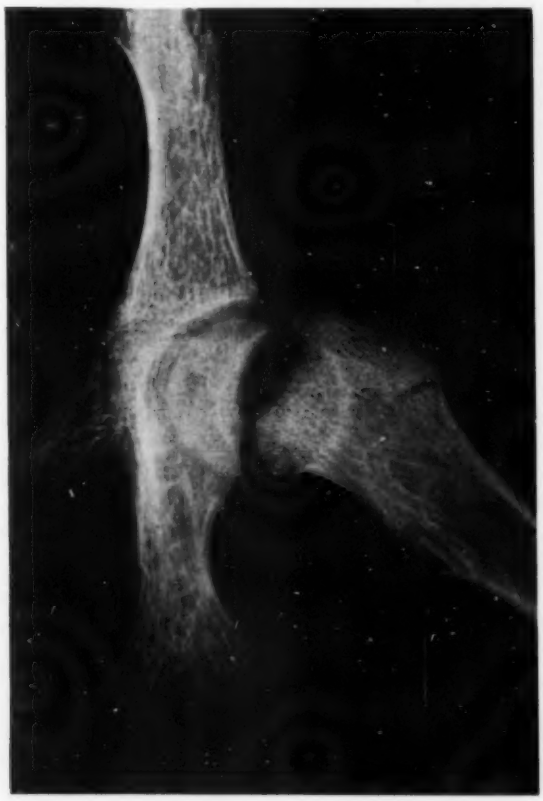

Fig. 12

Milch has admirably described this relationship as follows:

> This situation was readily comprehended as the visual expression of a fundamental proposition in projective geometry. The changing shadows represented the various projections of the roughly circular upper end of the femoral neck when exposed to the bundle of x-rays at angles varying from complete parallelism to complete perpendicularity. Once this was clearly established, it was apparent that the double shadow, observed in the roentgenograms of the monkey and of the children, was caused by the projection of two separate structures,—The upper end of the femoral neck and the lower or inferior surface of the capital epiphysis. The former cast the subcapital shadow; the

Fig. 14

latter, the capital shadow. For the purpose of calling to mind graphically the relationship which exists between the head and the neck of the femur, the acorn may be used as an example. The cup of the acorn represents the head, and that portion of the nut which fits into and is covered by the cup represents the upper end of the femoral neck. The circumference of each forms roughly a circular outline which is in the main concurrent, and which will cast a single shadow as long as both parts are in contact. However, when this fixed relationship is modified, so that the two circumferences are no longer concurrent—when the nut rotates out of the cup—it follows that the shadows cast by each will be independent and will vary in a manner depending upon the angle at which each circumference intercepts the bundle of rays. This is exactly the situation in the condition of epiphysiolysis. As long as the head is firmly fixed to the neck, both cast a single shadow, regardless of the position of internal or of external rotation in which the leg as a whole lies. However, once a separation occurs, both the upper end of the neck and the lower end of the head cast shadows which are independent of each other and which are related to each other only by a formula expressing their angular relationship to the line of the bundle of rays. Once these facts were completely assimilated, it was realized that therein lay the explanation of the so called progressive "widening of the epiphyseal line," which has been described as pathognomonic of epiphysiolysis. It became obvious that this "widening" represented not a true, but an apparent increase in the width of the epiphyseal line. It was evident that the increase in the width of the epiphyseal line was caused by the gradual anteversion of the neck and that the roentgenographic visualization of this phenomenon was phaselike, similar to the waning and waxing of the moon. This was confirmed by the facts that anterior displacement of the femoral neck could be demonstrated only in those cases in which there was an increase in the width of the epiphyseal line and that the degree of the anterior displacement seemed to vary directly with the increasing width of the epiphysis. It further accounted for Pomeranz's observation

Fig. 15

that "the roentgenogram usually shows a widening of the epiphyseal line which is best demonstrated when the hip is examined with the leg in external rotation."

THE ROENTGENOGRAM AFTER TREATMENT OF EPIPHYSEOLYSIS

The therapeutic maneuvers which are recommended for the treatment of this disease are designed primarily to realign the femoral head by either conservative or operative methods and to encourage its union to the neck by immobilization or rest. Thus it becomes the function of the roentgenologist to ascertain the success of these efforts.

The principle applied in the treatment of slight slipping is well defined. The desire is to prevent further slipping and in order to do so one attempts to hasten ossification at the epiphyseal line. The common methods are the use of the cast, with or without traction, manipulation, drilling and impaction with the Cotton mallet. In the cases of marked or chronic slipping, correction is attempted by manipulation, reconstruction operation, realignment of the epiphysis with wedge resection to correct the coxa vara deformity and subtrochanteric osteotomy.

Our previous experience with these methods will serve to illustrate what can be accomplished in this disease and likewise emphasize the significant roentgenographic changes which result from treatment.

Manipulation. Satisfactory reposition of the femoral head was accomplished in more than 50 per cent of the cases previously reported. The ultimate results were good. However, in many instances of bilateral slipping the untreated side heals as well as the treated side, particularly where inactivity is accomplished by rest in bed or by a plaster cast. In cases of chronic slipping, the condition is unaffected or made worse. In acute slipping, manipulation appears to be successful when performed within three months from the onset of the condition. On examination of the roentgenogram in many instances, however, the position of the alleged realigned head is frequently exactly what it was before manipulation. Even in the cases of slight slipping, some union may exist between the capital epiphysis and femoral neck, and in order to more satisfactorily realign the head, it would become necessary to convert the condition into an acute fracture. Occasionally an osteoplastic spur from the femoral neck impinges upon and prevents realignment of the epiphysis. There is also the danger that forcible manipulation may result in complete detachment of the head or severe trauma to the soft parts. The significance of the anterior rotation of the neck may not have been appreciated and in such instances, the coxa vara deformity is corrected but the anterior rotation persists as in the case above cited. The application of traction, with or without manipulation, likewise is frequently useless, because the upward displacement of the femoral shaft may be corrected but the rotation of the epiphysis would be wholly unaffected.

Drill Method. One of the advantages of the drill method is that it hastens union of the epiphysis to the neck and thus materially reduces the period of disability. As most of the growth of the femur occurs at its distal extremity, the premature fusion of the capital epiphysis and neck is of no consequence. It is important for the roentgenologist to determine whether the drill holes have been placed in a technically correct position. The channels produced by the drill are readily traced in the head and neck. It is perhaps best to take the roentgenograms in the operating room with the drills *in situ* for in this manner the accuracy of the procedure can be controlled. Roentgenologically, it is possible to demonstrate beginning fusion of the head and neck in about four weeks.

Cotton Mallet Impaction. Deliberate traumatization of the epiphyseal plate by impaction with the Cotton mallet also induces ossification through the epiphyseal line. Union, however, takes from four to

six months in the average case. The advantage of this method is that it is a conservative and effective approach to the problem. There is no specific roentgenologic picture which characterizes this method.

Realignment of the Epiphysis. In a few instances in which this operation was performed, the end-results were poor. Realignment of the head and neck is not so simple since the femoral head is often found either partially or completely united to the shaft. At best, however, the so-called realignment of the epiphysis is only partially successful; a residual deformity is present in many cases.

Wedge Resection, Realignment of the Head and Fixation with an Ivory Screw or Bone Peg. This is a somewhat radical procedure which occasionally leads to permanent contour deformities in the femoral head. The ivory screw or bone peg may be visualized in the roentgenogram for three or four years following operation, after which it is completely resorbed and fades out. However, realignment of the capital epiphysis at the time of operation may not be satisfactory and a residual coxa vara results or the trauma produced by curettage of the plate surface of the head produces marginal osteophytes.

Reconstruction Operation and Arthroplasty. These operations were performed on patients with marked slipping of more than six months' duration. In all the cases, the functional and anatomic end-results were poor. These operations are prone to result in a marked osteoarthritis, bony ankylosis of the hip joint or aseptic necrosis of the femoral epiphysis. They appear to be the least desirable of all methods to correct the deformity.

Osteotomy. In the cases of marked or chronic slipping, where union has resulted in a coxa vara deformity, subtrochanteric osteotomy appears to represent the totality of effective and permissible procedures to correct the deformity.

COMPLICATIONS AND SEQUELAE

Despite the simple character of the disease, complications are not infrequent. In one of our manipulated cases, the forceful maneuver resulted in a complete detachment of the hitherto partially slipped epiphysis. A similar accident followed Cotton mallet impaction. In another manipulated case, complete calcification of the capsule of the hip joint ensued. In the open operations, there is always the danger of infection, ankylosis of the hip joint or aseptic necrosis of the epiphysis. In many of the cases, the so-called good end-results, there are extensive changes in the contour of the femoral head and joint within five years.

CONCLUSIONS

1. Despite the frequency of epiphyseolysis, the condition is often unrecognized by roentgenologists, thereby seriously affecting the successful treatment of the disease.

2. Where clinical symptoms are suggestive, there are distinct roentgenographic features which indicate that slipping is taking place. There is therefore no preslipping stage of the disease.

3. In the early cases of epiphyseolysis, there is an absence of the projecting "hump" of the capital epiphysis, increased width of the epiphyseal line and subchondral resorption of the femoral neck.

4. In the moderately advanced cases, there is downward, inward and backward rotation of the femoral epiphysis. The femoral neck is anteverted.

5. Old cases represent the end-results of all stages of this disease where the epiphysis had united to the neck with residual deformity.

6. In some of the treated and all of the untreated cases, union of the capital epiphysis to the femoral neck in the slipped position leads to permanent changes which may be recognized late in life. Osteoarthritis is severe in the old cases and may lead to permanent ankylosis of the hip.

7. Utilizing the hip of a monkey, the different stages of the disease were experimentally reproduced and confusing shadows studied. It was found that the increase in the width of the epiphyseal line was in

reality produced by the progressive anterior rotation of the femoral neck. The crescentic densities noted in the roentgenogram represented the concurrent margins of the femoral neck and epiphysis.

8. The roentgenograms depicting the changes in the hip following different methods of treatment have been briefly described.

Grateful appreciation is herewith accorded to Dr. Henry L. Jaffe, Director of Laboratories at the Hospital for Joint Diseases, and to Dr. Henry Milch of the Orthopedic Service of the same institution, for their helpful suggestions and assistance.

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THE SIGNIFICANCE OF THE LATERAL VIEW OF THE RECTUM

A DESCRIPTION OF TECHNIQUE AND ITS VALUE

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ROENTGENOGRAPHIC examination of the rectum and sigmoid has been rather unsatisfactory because of the inherent difficulty of palpating and compressing

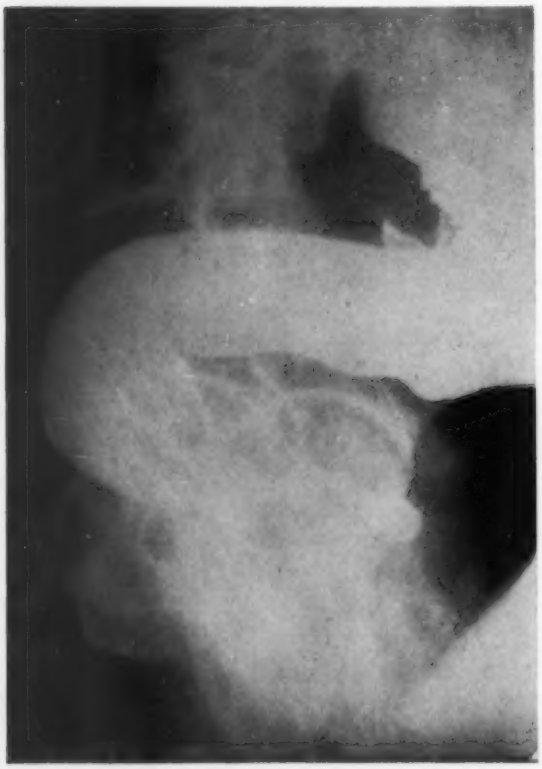

Fig. 1. A normal rectum as visualized by the lateral view.

these regions during roentgenoscopy. Thus, failure to visualize adequately these structures accounts for many of the errors in diagnosis.

The frequency with which lesions involve the sigmoid and rectum makes it a matter of great importance to develop more accurate methods of diagnosis. In view of the difficulties encountered in the roentgenoscopic approach, lesions on either the anterior or posterior walls may be completely obscured and their presence remain undetected.

For a number of years we have utilized the lateral and oblique views in addition to the routine positions. The lateral view (Figs. 1 and 2) is the more frequently used and has been of inestimable value in detecting lesions, totally unsuspected at the roentgenoscopic examination, because of the small size of the lesions or due to the overlapping of the sigmoid flexure.

The oblique position, described by Stewart and Illick,[1] is reserved for those instances where lesions are suspected or visualized at the roentgenoscopic examination.

The routine use of the lateral position has resulted in the detection of small lesions and the extent of the larger deformities (Figs. 3, 4, 5 and 6). This valuable method of examination, although mentioned in the literature of Kantor[2] and Fricke,[3] through its paucity indicates an insufficient cognizance of its value.

In reviewing the anatomy of the rectum, we find that it begins at the level of the third sacral vertebra and follows the curve of the sacrum and coccyx in its descent. Just beyond the coccyx it rests on the pelvic floor and turns abruptly downward and backward into the anal canal. The rectum is curved in both the anteroposterior and lateral planes. In the anteroposterior view it is seen to zigzag from side to side, varying somewhat with different in-

Fig. 2. Normal lateral views before and after evacuation. In this instance the sigmoid is partially obscured by a redundant loop. The mucosal relief of the rectum is well shown in the film after evacuation.

Fig. 3. A small malignant lesion at the posterior wall of the proximal portion of the rectum. The diagnosis was substantiated by biopsy. The patient, a male, aged forty-two, had a large nodular liver, containing metastasis. This was demonstrated after the administration of thorotrast. We believe that this type of lesion is usually not detected by methods commonly in use.

Fig. 4. Extensive carcinoma of the rectum. The location and extent of the lesion are well outlined.

Fig. 5*A* (Retouched). Carcinoma of the rectum just proximal to the anus in a patient aged twenty-three.

dividuals; but in the main it is seen to have three distinct curves: a proximal and distal one, bearing to the left, and a central, bearing to the right. In viewing the rectum from its side, we note that it forms a gentle curve with its convexity posteriorly, fitting into the hollow of the sacrum and coccyx. Wolf,[4] in his study of the anatomy of the rectum, utilized the lateral view. He believed that the rectum could best be demonstrated with the patient in the erect po-

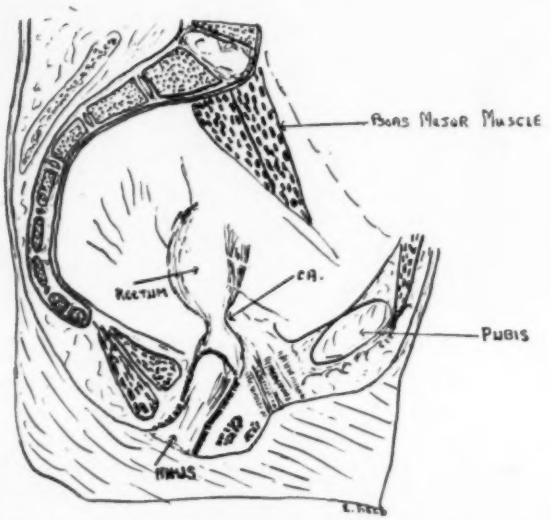

Fig. 5*B*. Median section (schematic) to illustrate Figure 5*A*.

sition. He states that the appearance of the rectum in the lateral view is totally different from that of the anteroposterior or posteroanterior views. In the standing position, the rectum descends as a banana-shaped, smooth-walled tube, and he regards the so-called ampulla as being due only to the convolutions of the rectum. He shows the rectum proceeding first toward the right, then forward and to the left, and back toward the right.

In 1930 Wolf[4] studied the anatomy of the rectum roentgenographically, utilizing the lateral position. In a subsequent report he[5] presented a study of various pathological lesions demonstrated in the lateral view. In applying this method to examination of the splenic flexure and descending colon (Figs. 7 and 8), we have noted on

Fig. 6 (Retouched). Annular carcinoma of the rectum, well demonstrated in the lateral view.

Fig. 7. Carcinoma of the splenic flexure. The lesion was obscured in the posteroanterior film by a redundant loop.

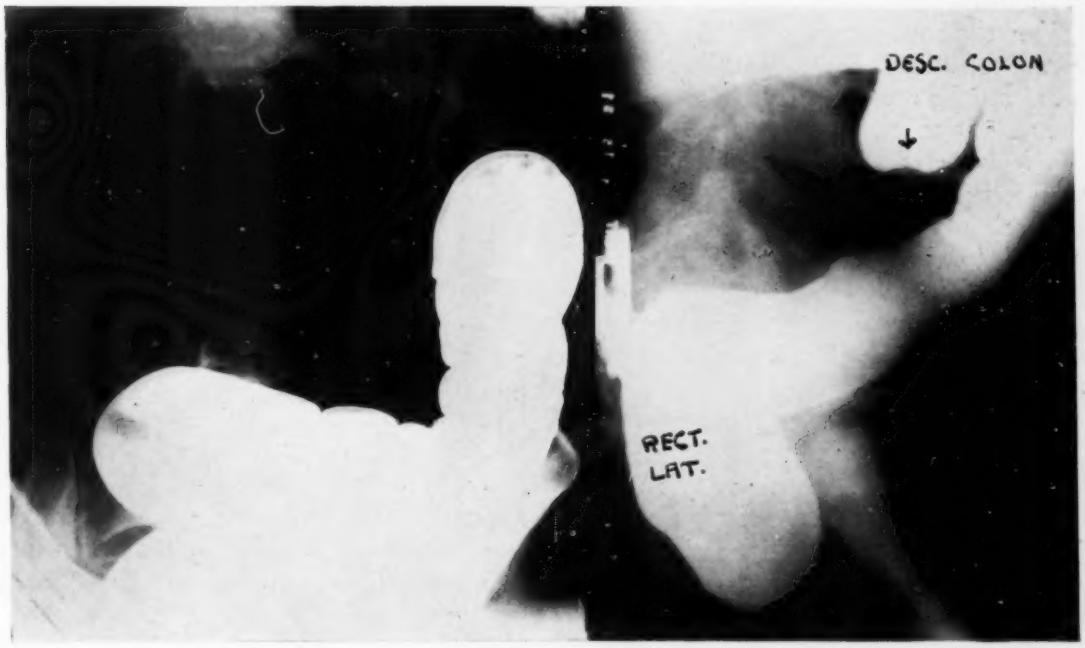

Fig. 8. Carcinoma of the descending colon. Due to the redundant loop, the exact nature and location of the lesion are obscured in the posteroanterior view. Both are well shown in the lateral view.

Fig. 9. A normal right lateral view. Note the pseudo filling defect caused by the convolution in the rectum.

occasion a better demonstration of lesions involving these regions than that portrayed by the usual routine.

TECHNIQUE

After the routine preparation of the patient as for a barium clysma, the patient is placed on the roentgenoscopic table in the prone position, a rubber or metal rectal tube is inserted about 4 inches into the rectum, the shut-off is then released and the barium mixture is allowed to flow slowly into the rectum with a minimum amount of pressure, carefully observing under the roentgenoscope the distention of the rectum and the advance of the opaque column into the sigmoid. The patient is instructed to turn first to the left oblique position, then to the right oblique position, and then to a true lateral position. The flow of the clysma is frequently interrupted in order to study small sections of the lower bowel. The entire colon may thus be filled gradually and studied carefully.

A

B

Fig. 10, *A* and *B*. Narrowing of the sigmoid secondary to a pelvic tumor. Note the preservation of mucosa in both the anteroposterior and lateral views. No pathology in the rectosigmoid.

After the roentgenoscopic observations have been completed and the most adequate position to outline the lesion determined, films are taken to outline the entire colon with the prone and oblique positions. The patient is then placed in the left lateral position and another exposure is made. In routine practice we find that the left lateral view is the most satisfactory because in the right lateral position there is often seen a pseudo filling defect of the rectum in its midportion due to one of the convolutions (Fig. 9). This view is taken with the rectum fully distended with the clysma.

Films in the lateral position after evacuation are also helpful in demonstrating the mucosal pattern of the rectum and occasionally of the sigmoid (Figs. 2 and 10).

Fig. 11. Carcinoma at the rectosigmoid junction. Note how clearly the caliber of the lumen is demonstrated.

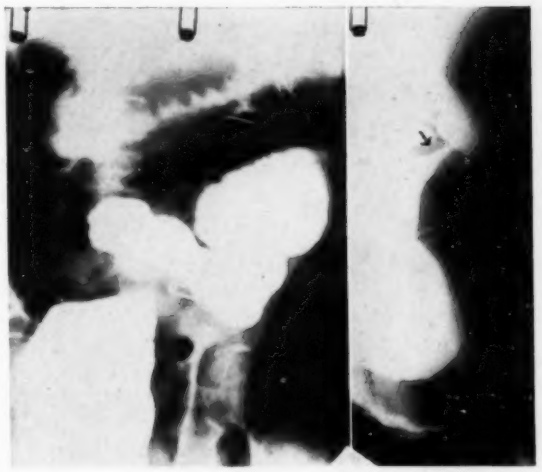

Fig. 14. Concentric narrowing of the sigmoid, secondary to a pelvic abscess, in a patient, aged sixty. This abscess formed after an operation. A previous barium enema, just prior to operation, was negative.

Fig. 15. Carcinoma of the rectum. Note the diverticula at the posterior wall of the sigmoid and descending colon. These were not visible either roentgenoscopically or on the usual films.

In difficult cases when the patient cannot retain the enema or when the patient is uncooperative, a low enema by just filling the rectum will facilitate the exami-

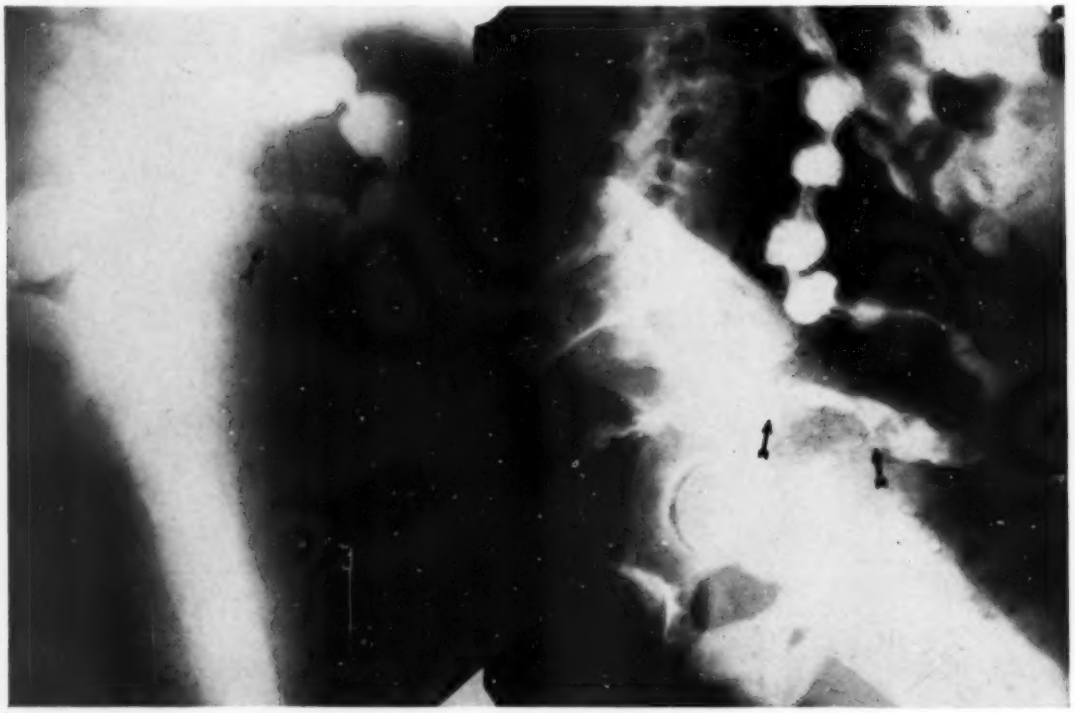

Fig. 12. Carcinoma of the sigmoid. The abrupt change in the mucosal relief is well demonstrated on the film after evacuation

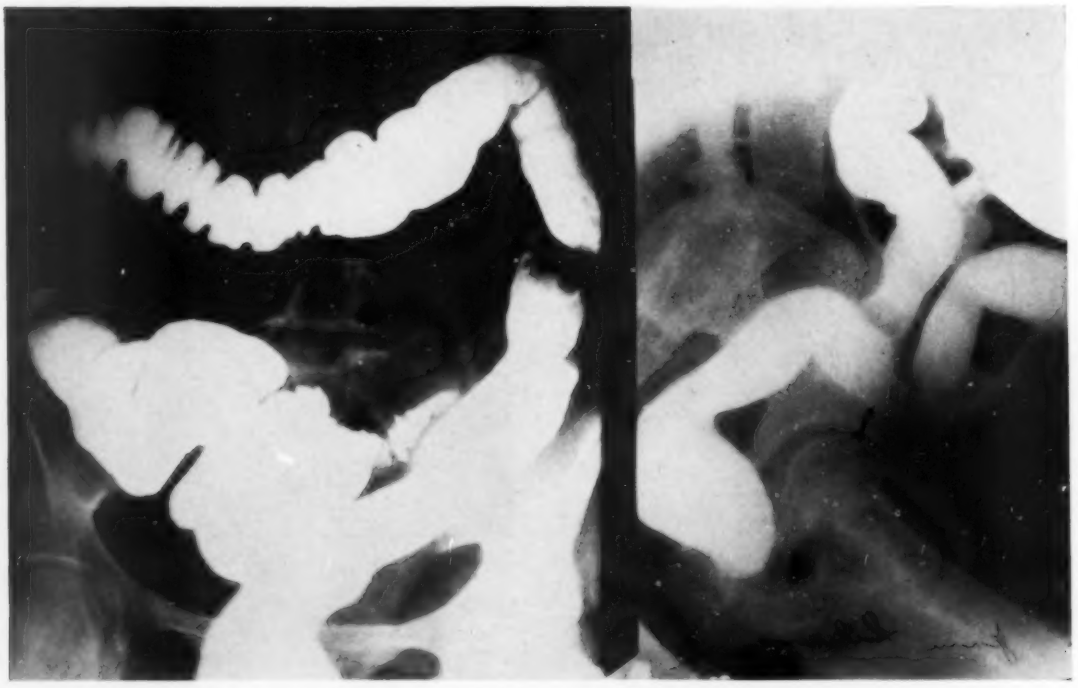

Fig. 13. Annular carcinoma of the sigmoid. This lesion was not seen roentgenoscopically and was obscured (by redundant loops) on the routine films. The barium enema was being done as a routine procedure; clinical diagnosis—cholecystitis!

nation, and the presence or absence of a lesion in the rectum can thus be determined.

The diagnostic value of the study of this region by this procedure is enhanced by our ability to demonstrate small lesions on the anterior and posterior walls which by the ordinary methods are obscured. In addition, the extent of the larger lesions is more easily discerned.

This method also contributes in ascertaining more accurately the size of the lumen as influenced by strictures, by benign or malignant lesions (Figs. 11, 12 and 13); it enables us to follow the various changes in the lumen subsequent to pressure produced on the rectum or sigmoid by extrinsic causes (Figs. 10 and 14), or those due to inflammatory disorders, such as colitis, diverticulitis, and abscess. Fistulous tracts present themselves more easily. Diverticula at either the anterior or posterior walls, often not visualized on routine films, are better demonstrated.

SUMMARY

The routine use of the lateral views of the rectum and sigmoid is urged inasmuch as a greater percentage of correct diagnoses of diseases of the colon will result. Any simple method which can reduce the roentgenologist's percentage of error should certainly be included in his diagnostic armamentarium.

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SUBARACHNOID ALCOHOL INJECTION FOR RELIEF OF BRACHIAL NEURITIS

USE OF LIPIODOL PRELIMINARY TO HIGH SPINAL ALCOHOL INJECTION*

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DETROIT, MICHIGAN

INTRASPINAL (subarachnoid) injection of alcohol has not been done very often for the relief of pain in the upper extremity. There is danger of alcohol extending up to involve the medulla if the head is not kept low and horizontal. Nevertheless there are often cancer victims with severe, excruciating brachial plexus pains who may be benefited by this procedure. Rather than the risks of high chordotomy or the drawbacks of chronic morphinism, subarachnoid alcohol injection may be the method of choice in such debilitated individuals, whose life expectancy is uncertain and the safety of major operation doubtful.

There is also the technical difficulty that, at times, in such patients, there may be little or no spinal fluid in this region. The spinal cord is much closer to the dura here than in the lumbar area, hence a small disturbance (old adhesive pachymeningitis, marked dehydration) may result in a dry tap or injury to the cord by the lumbar puncture needle. The needle may be in the subarachnoid space and no fluid obtained. Injection of alcohol is then dangerous because of too great concentration if not diluted with spinal fluid. The dry tap obtained in the first case, made one of us (F.S.) decide to introduce a few drops of ascending lipiodol into the canal before injecting alcohol. Under the roentgenoscope, one can then determine whether the needle is in the subarachnoid space by the movement of the lipiodol.

Another technical difficulty is that there may be considerable variation in the anatomic relations of the bony skeleton and the spinal canal; arthritis, dorsal curvature, depth of canal beneath the skin, etc., may cause the needle to enter at another point than that desired, or the alcohol be introduced at an angle, and ascend or descend beyond where it should. By placing the patient on a tilt table, this can be more accurately controlled. This is especially valuable in high dorsal injections where accurate placement of the alcohol is necessary.

Technique. The patient is placed on a tilt table. Arching the site of injection with a pillow, pushing the patient somewhat ventral-ward are the same as for usual spinal alcohol injections.

The needle is introduced at the desired level. Under roentgenoscopic control, one drop of ascending lipiodol is injected. The position of the lipiodol is ascertained. If it is not lying in the region of the nerve roots which it is desired to bathe, the table is tilted either up or down until it is exactly in the right place.

The following 2 cases are reported to illustrate the usefulness of lipiodol injection preliminary to high alcohol intraspinal injections; also to call attention to the value of high alcohol injection for the relief of intractable pain in the upper extremity.

Case 1. B. R., female, married, aged forty-eight, bedridden for eighteen months. Carcinoma of breast with extensive spinal metastases. Girdle pains in upper chest. During several months' observation the location of the pain changed several times, apparently with varying pressure, etc., inside the spinal canal.

Intrathecal puncture in third dorsal interspace brought forth no fluid. A few days later, puncture was made in the space above. A droplet of ascending lipiodol was introduced. Under the roentgenoscope it was seen to move enough to be sure that the needle was in the canal, but no fluid escaped. Alcohol was therefore not injected, and further attempts not made.

* From Harper Hospital and Mercy Hall Tumor Clinic and Hospital.

Case II. E. M., female, married, aged fifty-four; severe brachial neuritis from pressure of a supraclavicular mass secondary to carcinoma of the breast.

The patient cried out at intervals because of the excruciating pain down the forearm. She held her arm on a pillow, and would not let the nurses change her position because of the severe pain which any movement caused. Stroking the ulnar border of the forearm or back of the hand might initiate a violent spasm of neuralgia up and down the arm. The hand was edematous, practically useless. She required 2 grains of pantopon in twenty-four hours.

On December 10, 1937, spinal puncture was made into the dorsal interspace between the third and fourth spines. A few drops of ascending lipiodol were introduced, under the roentgenoscope, and seen to flow freely at the site desired; 0.75 cc. absolute alcohol was injected. Patient remained on left side. Immediately after the injection pain was 75 per cent relieved. Next morning, the forearm and hand could be touched without discomfort. This permitted nursing care of the patient, which was very difficult before. The edema of the hand and arm gradually subsided, starting within twenty-four hours. In three weeks it was all gone. It never returned.* There was some improvement in motion of the hand—she could move her fingers—but could not grasp with her hand. She was now comfortable under 1 grain of codein. After two weeks, and after being moved away from another patient who was given hypodermic injections of morphine frequently, she required practically no drugs. She did not need pillow rest for her hand. She turned on her side voluntarily. She still craved drugs, but would go to sleep for long intervals under a sterile hypodermic.

She was comfortable until February 10–15, 1938. Then she developed increasing cough, slight rise in temperature and signs of pulmonary metastasis, and died two weeks later (February 24, 1938). The pain in the arm had been completely relieved to the time of death (two and a half months).

* Stern (Stern, E. L. Intraspinal injection of alcohol for relief of pain and for sympathetic nervous system disorders, *Med. Rec.*, 1936, *143*, 327) has noted that intraspinal alcohol injections may have a therapeutic value in peripheral vascular disease. By paralyzing the afferent sympathetic fibers, the same vasodilatation which follows sympathectomy, ganglionectomy, etc., may ensue.

NOTE ON THE REDUCTION OF BACK-SCATTER FROM ROENTGEN BEAMS

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IN ROENTGENOGRAPHY and roentgen therapy use is made of a beam of radiation usually defined by an aperture of lead. A certain amount of the energy of the beam is utilized, a certain amount unavoidably scattered, and the remainder goes on its way as a direct beam to be finally scattered and absorbed by the walls, floor and ceiling of the room, or in lead or other screens interposed in its path. If screens are used close up to the point where the beam does its useful work, the amount of back-scatter is usually enough to act back on the film or patient, as the case may be, giving undesired results. The usual practice is to let the beam strike a wall, ceiling or floor surface far enough from the film or patient so that the back-scatter is negligible. This fills the whole room with scattered radiation, requiring careful protection of the whole room to prevent cumulative injurious effects to the operators continuously exposed. In this note we describe a construction of screen that can be put in the direct beam, close up to the patient or film with a sufficiently great reduction in the radiation scattered back from the screen to enable either the amount of protection to the operator to be cut down considerably, or for the same protection, a great increase in the factor of safety. This increase in safety can be obtained inexpensively and should be of wide applicability.

The screen depends for its operation on the fact that radiation scattered from any

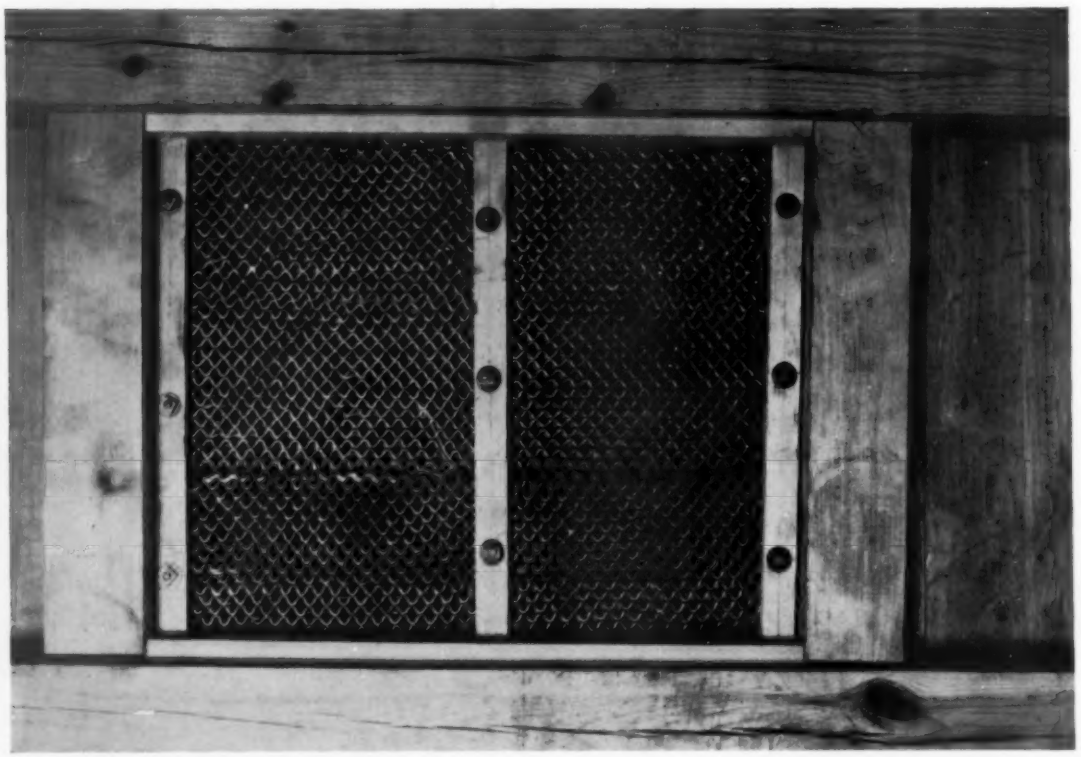

Fig. 1. Photograph of back-scatter grid in ceiling of treatment room; 600 kv. installation at Harper Hospital.

material, is, at all common voltages, scattered in all directions while the beam is nearly parallel. This means that if a cellular construction of absorbing material is made with the axes of the cells in the direction of the beam, most of the beam will pass through the cellular grid. However, if a flat sheet of absorber is placed on the far side of the grid, most of the scattered radiation from this sheet will strike the walls of the cells, being reabsorbed and scattered. The combination of the grid and sheet acts as a trap for the beam.

Figure 1 shows a home-made beam trap designed for use on the high voltage (600 kv.) therapy machine at Harper Hospital. It is shown as mounted in the ceiling of the treatment room, where it is out of sight under the finish, and has been in use for nearly two years.

The optimum design for thickness of lead and size of cells is somewhat different for lower voltages. The thickness of the walls of the cells in this trap is 1/16″, the cells are ¼″ square and 1″ in depth. The

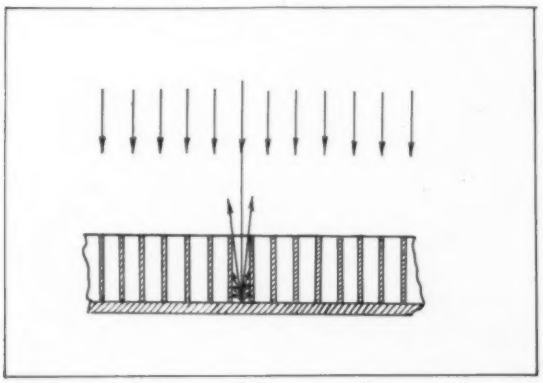

Fig. 2. Vertical cross-section of cellular grid.

sheet on the back which is an integral part of the trap is ⅛″ thick, but this is backed up by an additional inch of lead in this installation. The beam trap can be made still more efficient by making the cells deeper and of smaller cross-section, but there are practical limits to this procedure.

Figure 2 is a diagrammatic section of the grid, showing how the scattered radiation at different angles strikes the walls of the

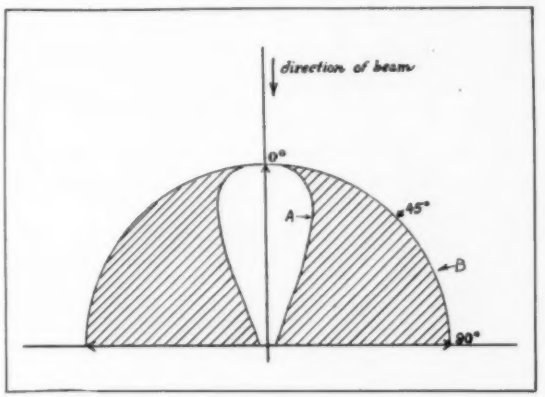

Fig. 3. Back-scatter intensity curves at 200 kv.

cells. A small cone of scattered radiation, directly back toward the original beam, will be unimpeded. The percentage of the total on the grid shown in Figure 1 is approximately 10 per cent; in other words, it cuts out about 90 per cent of the total back-scatter. Actually it is a little less than this, as some scatter comes from the ends of the cells, and some rescattered radiation will find its way out of the trap.

Figure 3 shows the angular distribution of the back-scatter from the grid (curve *A*) and the distribution if there were no grid (curve *B*). Measurements were taken with the grid, and simply by covering the grid with lead to get the total back-scatter. The volume of the hemisphere formed by rotating the figure about its vertical axis is proportional to the total scatter without grid. The volume of the region formed by similar rotation of the shaded portion is proportional to the back-scatter eliminated. The ratio of these volumes is much greater than the ratio of the areas.

THE PHOTO-ELECTRIC DENSITOMETER*

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IN RECENT years, considerable attention has been devoted to the development and application of an electro-optical technique for the accurate determination of roentgenographic film densities. A need for such measurements seems to have been generally recognized, and several investigators have already published descriptions of successful apparatus. Each of these reports shows individual merit and originality of design, although such originality would of itself seem to indicate a wide difference of opinion as to what constitutes the most desirable equipment for the purpose. The roentgenologist who wishes to assemble a densitometer suitable to his own needs, but who has not the time nor the inclination for extensive study and research in basic principles, is apt to become confused by the very multiplicity of available designs.

In view of these facts, a discussion of the relative advantages of some of the representative types seems to be in order. For the background of such a discussion, certain direct comparisons have been made in this laboratory, with special attention devoted to the following factors:

1. Accuracy sufficient to insure reliable results.

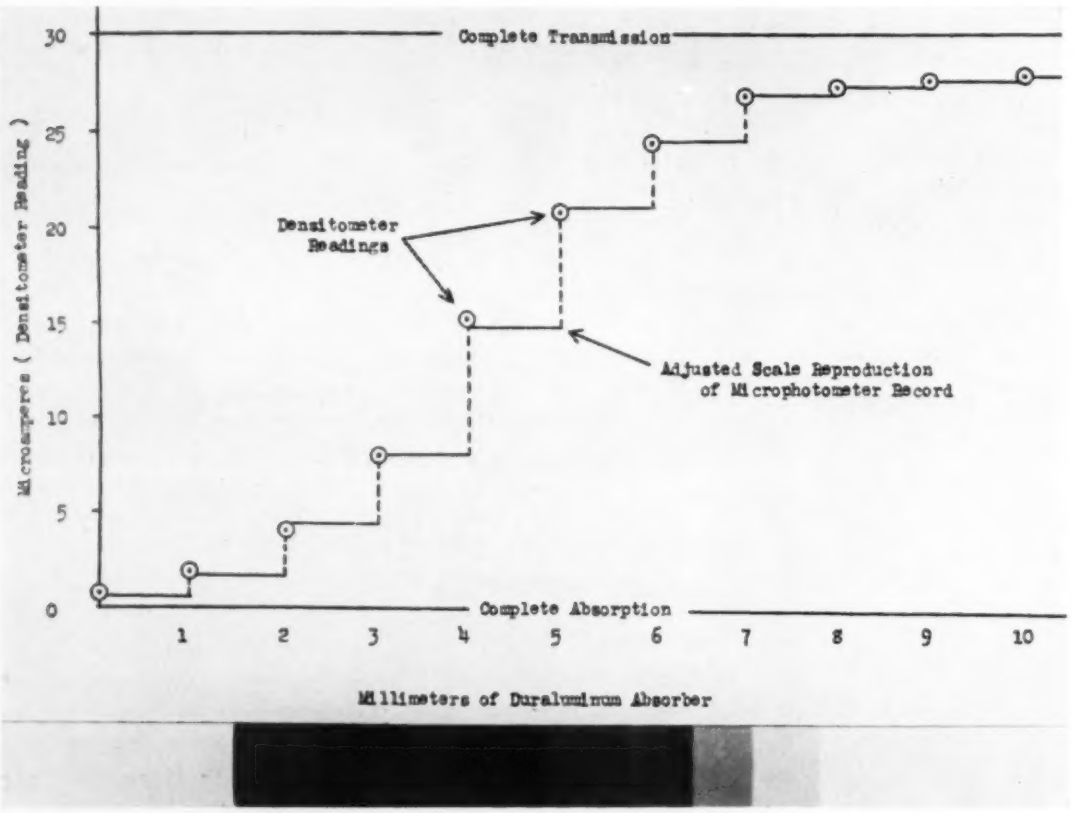

FIG. 1. Comparison plot of densitometric data vs. standard microphotometer record of density strip reproduced below.

* From the Department of Radiology, Duke Hospital.

2. Constant sensitivity during any series of readings.
3. Maximum flexibility and speed of manipulation.
4. Simplicity and low cost of initial construction.
5. Lack of troublesome maintenance or re-calibration.

Our problem, then, is to attempt to select the particular assemblage of components which will most nearly meet all of these qualifications.

CRITERIA OF ACCURACY

The standard chosen as a basis for comparison and calibration of the apparatus under analysis was the Moll microphotometer. This is a research instrument of recognized precision, intended for highly accurate measurements of density over relatively minute areas. In general principle it is closely analogous to the simpler densitometers, but its high cost and somewhat cumbersome operation make it difficult to apply in routine roentgenographic work. Although such extreme accuracy is unnecessary in the case of the ordinary roentgen film, whose relatively coarse emulsion grain sets a very definite limit to the degree of precision attainable, it has served admirably in the capacity of a reference standard. On this basis, the reliability of each of the circuits assembled for comparison was checked on average measurements of a series of density steps, whose values had been previously established from the microphotometer records. A representative sample of such data is reproduced herewith (Fig. 1).

It is only fair to state, however, that while some of the circuits were found to require more painstaking adjustment and greater precautions against error than others, each one of the series has proved inherently capable of entirely satisfactory accuracy. Since none of the apparatus tested can be eliminated for failure in this respect, relative merit ratings must be referred to other factors less tangible.

FUNDAMENTAL PRINCIPLES

Of the various types investigated, all are found to consist essentially of the following units:

1. A source of illumination, designed to pass an intense beam of light through the film.
2. A device for converting the transmitted light into a proportionate quantity of electrical energy.
3. A means of measuring this electrical output.

THE SOURCE OF ILLUMINATION

For the source of illumination, most investigators have agreed in the use of a low voltage, narrow filament bulb of the automobile headlight variety. A very simple lens system is usually sufficient to focus this illumination to a brilliant spot. Although it is essential that the intensity of the light source remain constant during any reading, voltage obtained from the power lines is rarely steady enough for even approximate accuracy. For this reason, most densitometric equipment has been designed to use lead storage cells for filament supply. Such batteries are inexpensive, and are inherently stable in voltage over most of their discharge cycle. The common practice of placing a rheostat in series with the lamp for control of sensitivity is, however, of questionable merit. Even the best of variable resistors shows some change with temperature and unless careful check is kept with an ammeter in the filament circuit, and compensating adjustments made as heating takes place, considerable drift may occur during the readings. It has been found that a variable shunting resistance across the cell or the indicating meter, where the current is too small to cause any appreciable heating effect, offers a more accurate and less troublesome method of sensitivity control.

While the storage battery is recognized as a reliable and simple source of current, its bulk and weight make the apparatus

rather cumbersome if any degree of portability is desired. Under certain conditions, the necessity of frequent re-charging may also be an undesirable factor. In such cases, satisfactorily steady current for the lamp may be obtained from the power lines by the use of one of the several tried and proved automatic regulator circuits. One

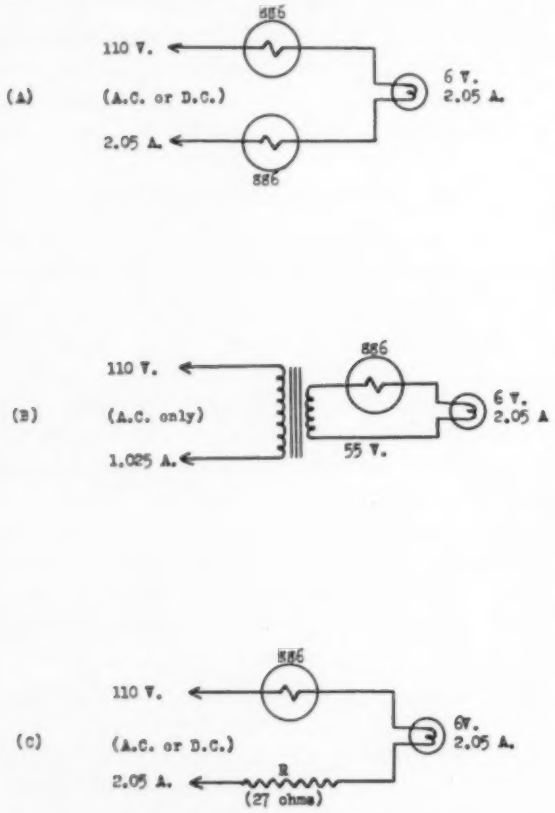

Fig. 2. Some optional ballast circuits for constant current supply.

of the most effective methods of obtaining such stabilization is by the proper application of the commercial "ballast tube," many types of which are now on the market. These devices in general consist of a filament having a high temperature coefficient of resistance, enclosed in a gas-filled envelope for protection and thermal regulation. Variations of the line voltage from its normal value cause corresponding changes in the temperature and consequent resistance of this filament, thereby tending to absorb such fluctuations within the ballast tube and maintain the lamp current constant over a rather wide range of supply voltages. In the present experiments, for example, two R. C. A. type 886 regulators in series with a 6 V. 21 C. P. headlight bulb (Fig. 2, *A*) were found to maintain completely satisfactory stability over an input range of 105 to 120 volts. Surges beyond these limits are not likely to be encountered in the average locality. Good results are also possible with a circuit using only one tube, by the introduction of a suitable transformer (Fig. 2, *B*) or simply a series resistance (Fig. 2, *C*). The accuracy of regulation is naturally somewhat less in these instances, but will be found adequate for most conditions. Since the characteristics of the various manufacturers' ballast tubes vary widely, the proper voltage and current relations must then be computed for the particular one chosen. The figures given above are of course valid only for the type mentioned.

There are likewise available some very effective ready-made stabilizing devices, which operate on the principle of the saturated core transformer. While these are definitely superior in mechanical ruggedness and resistance to abuse, they are usually more bulky and expensive than ballast tube circuits providing comparable efficiency of regulation. The choice should rest with individual preference.

THE PHOTOSENSITIVE UNIT

The next important decision is that of the proper type of light-sensitive device. These fall into two broad classifications: the so-called "variable resistance" cells which require an external source of electromotive force for their operation, and the "self-generating" type which actually convert light energy directly into electrical energy. This feature, by dispensing with some of the auxiliary circuit, tends to simplify the entire apparatus.

Under the first mentioned group may be listed the highly accurate vacuum cells usually employed in precision research applications. These have the disadvantages of extremely large internal resistance,

which necessitates the use of an amplifying circuit or other delicate (and frequently unstable) methods of output measurement. Next, the gas-filled emission cells are essentially modifications of the vacuum type. These are slightly less accurate, but have a somewhat greater output rating. More convenient than either of the above are the newly improved models of the original selenium cell, which have a resistance low enough to be used with only a moderately sensitive meter. The necessity for an external polarizing circuit, however, may constitute a serious drawback from the standpoints of simplicity and portability.

It is apparently most desirable, then, to employ a self-generating cell if the minimum of auxiliary equipment is to be realized. First among this group should be mentioned the thermopile. The sensitive element of the standard microphotometer previously mentioned is of that classification, and certainly in the matter of accuracy it leaves little to be desired. The current generated is rather small, however, requiring a delicate galvanometer which is not readily portable, and furthermore the cost of a good thermopile is usually rather large.

Let us consider, then, the copper oxide and the "barrier layer" cells, such as the Langé, and the domestically manufactured photronic type. The accuracy of these cells, although less than that of some of those previously mentioned, is found to be more than ample for roentgenographic applications. In our final instrument, we have employed the Weston photronic cell—principally on account of its availability and reasonable price. Its output has been repeatedly checked against precision standards over a period of several months, and the results have been consistently satisfactory. Due to the relatively large current available from this cell—1.4 microamperes per lumen—it was found that a portable low resistance microammeter of 0–30 U. A. range was amply sensitive for all readings, while a single 1-inch flashlight lens proved adequate for the light focussing system. The general simplicity of the final layout is shown by the schematic diagram of Figure 3 and the photograph of Figure 4. The comparison of data from this instrument with the Moll microphotometer records, as previously shown in Figure 1, is indicative of the accuracy to be expected. Only one precaution

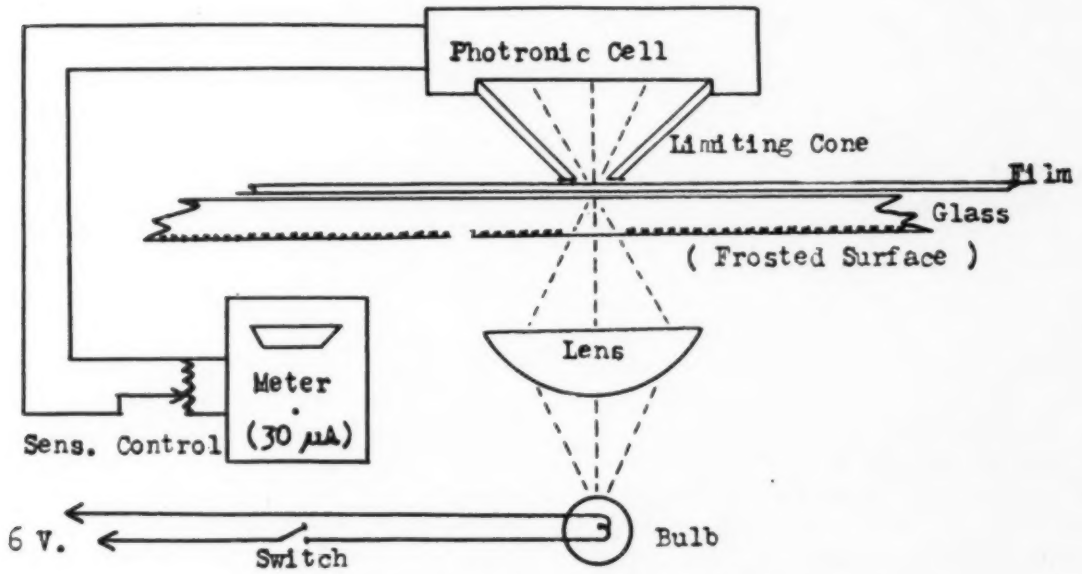

Fig. 3. Schematic diagram of improved apparatus.

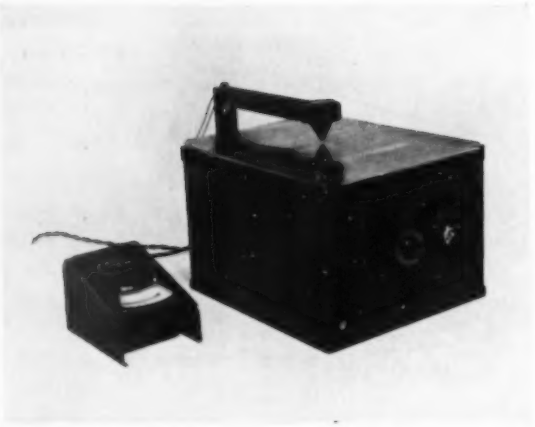

Fig. 4. Photograph of densitometer in use.

is necessary in order to realize this maximum precision: the operator must wait a few seconds before taking each reading, until the current reaches its equilibrium value. Under average conditions, a sufficient time interval will be expended in adjustment and preparation for recording the reading, without any deliberate delay being necessary.

No particular originality is claimed for this design. It is presented merely as a composite of the most desirable features of its various predecessors, together with a few of our own suggestions for further improvement.

DISCUSSION

The basic principles of densitometric measurement have already been adequately summarized in the work of Weyl and Warren,[1] Henny,[2] and others. Incidentally, it should be noted in this connection that the instrument described by Henny already includes several of the important features emphasized in our own selection of apparatus. We have found it desirable, however, to make certain basic departures from the design and methods of application of this, as well as other such devices previously discussed.

In the first place, we prefer to eliminate the battery rheostat, for reasons stated in an earlier paragraph, in favor of a sensitivity control in the cell-and-meter circuit. Moreover, it is obvious that the handling and orientation of films on the densitometer table will be greatly facilitated if provision can be made for their illumination by transmitted light. For this purpose, we have reversed the usual arrangement of the light and the photosensitive unit by placing the source of illumination with its focussing lens below the film (Fig. 3), while the cell and associated equipment are mounted above. The frosted glass surface which is used in place of the conventional bakelite or aluminum table of former designs permits an adequate, uniform illumination of the film by means of scattered and otherwise wasted light from the source. The necessary definition or limiting of the area scanned is accomplished by means of a conical shield which is attached to the cell and rests directly on the film. The small aperture in the apex of this cone is located in coincidence with the spot of maximum brightness at the focal point of the lens. A hinged bracket allows the entire assembly to be tilted back out of the way for unobstructed access to the table.

In order to provide a fixed standard of density by which any film may be accurately compared with any other, it has been found desirable to include a "density ladder" record on all routine plates. A small "penetrometer" made up of ten steps of 1 mm. duraluminum is provided for each roentgenographic room. This is placed on a corner of the cassette, along with the regular identifying numerals, whenever an exposure is to be made. With such a permanently recorded standard, it becomes a simple matter to plot the complete emulsion sensitivity curve of the film, or to state the density of any portion directly in terms of its equivalent thickness of metal. This latter feature, being independent of variations in exposure and development technique, is of particular value in following through a sequence of diagnostic plates, as for instance in the recovery and recalcification of rachitic bones or in studies of the rate of concentration

and elimination of various artificial contrast media in the organism.

The final model of our instrument as herewith described has also been applied to some experimental investigations of the problem of roentgen-ray absorption curves from roentgenographic data, by the methods of Glasser and Rovner[3] and of Meyer.[4] The results have been entirely satisfactory so far as the accuracy of the densitometric measurements were concerned, and the data thus obtained have been found to agree closely with the Glasser-Rovner curves.

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TRAUMATIC MALACIA OF TARSALS AND METATARSALS

CASE REPORT

By C. W. BRAINARD, M.D., *and* W. O. UPSON, M.D.
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WE WISH to report a case of clinical and roentgenological changes in the foot, similar to those reported as "march foot." We feel this case has other characteristics which may add to the theory that these changes are due to oft repeated mild traumas which produce a disturbance in the blood supply of the part, with consequent disturbance of the nutrition of the bones.

Speed and Blake[1] have reported 9 cases, with a review of the literature, and call attention to the disturbance in function of the anterior metatarsal arch as an etiological agent. Improper weight bearing in these cases produces the repeated trauma which causes the interference with blood supply by producing a myositis and fibrosis of the intrinsic muscles attached to these metatarsals.

FIG. 1. An irregular translucency of the cuboid, cuneiforms, and scaphoid, and the distal end of the first metatarsal.

Köhler[2] mentions the possibility of bac-

[1] Speed, J. S., and Blake, T. H. March foot. *J. Bone & Joint Surg.*, 1933, *15*, 372–382.

[2] Köhler, A. Röntgenology: The Borderlands of the Normal and Early Pathological in the Skiagram. William Wood & Co., New York, 1928.

Fig. 2. Condition one year after first examination showing nearly normal bony contour except for a small area of cortical thickening in the distal end of the fourth metatarsal.

terial invasion embolic in origin, producing a periosititis and bone necrosis. Clinically, there is a gradual onset of pain in the forefoot, accompanied by swelling. Roentgen changes are not evident until several weeks have elapsed, then there is the periosteal thickening of one or more of the metatarsals, usually the second, third or fourth, and later there may be callus formation if a true fracture occurs.

The case we wish to report differs from the usual description in that all of the bones of the forefoot were involved. A brief résumé is here given.

W. O. U. (one of the writers), aged fifty, occupation roentgenologist, had gradual onset of pain in the right foot on weight bearing. This was accompanied by swelling of the dorsum of the foot. There was no history of injury and the condition was thought to be an acute foot strain. Examination showed a long narrow foot with moderate relaxation of the anterior metatarsal arch, swelling of the dorsum of the foot, pain on palpation of the tarsometatarsal and metatarsophalangeal joints, and pain on motion both active and passive of these joints. Roentgen examination was entirely negative. The type of shoe worn by the patient was evidently too short and narrow, and this was corrected. No relief was obtained and in six weeks, a further roentgen examination was made with the changes evident in Figure 1. There was proliferation of the periosteum of the second, third and fourth metatarsals, and in addition there was a loss of the normal contour of the tarsometatarsal joints with a decalcification of the cuboid, cuneiforms and scaphoid, and the distal end of the first metatarsal. This decalcification did not give the impression of an osteoporosis, but more of an irregular translucency of the bone. Immobilization of the foot in a plaster boot for six weeks was done, followed

by baking and massage and the symptoms subsided, weight bearing being resumed in about ten weeks. No return of the symptoms have been noted and a roentgenogram taken one year later (Fig. 2) shows normal bony contour, except for a small area at the distal end of the fourth metatarsal which shows some cortical thickening. This may well be the site of fracture with callus formation.

The involvement of other bones of the foot than the metatarsals prompted us to report this case, and we believe the condition lies in the same category as the so-called "traumatic malacia" of the carpal bones described by Köhler. He believes that there are changes in the semilunar first described by Kienböck, which may be the result of continued compression injuries, occupational in origin, and with a resultant disturbance of the blood supply, producing a decalcification and loss of normal contour of the bone. In this particular case, poorly fitting shoes and continuous weight bearing on unpadded floors could well be the cause. Immobilization was sufficient to produce relief of symptoms, and a well fitting shoe seems to have prevented its recurrence.

CASE REPORT FROM THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS

Edited by JAMES R. LINGLEY, M.D.

CASE 109872. A female, aged sixty-two, married, American, entered the hospital because of abdominal cramps and vomiting of two and a half months' duration. The abdominal pain came on in attacks every one to two weeks and lasted three to four days. It was generalized and definitely cramp-like in character. Her abdomen became distended during the attacks and she had occasional vomiting. She had daily bowel movements, but on several occasions she noticed streaks of blood in the stools.

Physical examination revealed a well-developed, obese woman, in moderate distress. The abdomen was greatly distended, tympanitic and diffusely tender. There was dullness in the flanks with no demonstrable fluid wave. No masses were felt. Rectal examination was negative except for external hemorrhoids. Pelvic examination revealed no abnormalities. The temperature was 99° F., the pulse 92, respiration 20, and blood pressure 118/82. Laboratory findings: red blood count, 4,960,000; white blood count, 10,400; 89 per cent polymorphonuclears. Urinalysis negative. Non-protein nitrogen 34 mg. per 100 cc. Chloride 110 cc. N/10 $Cl.CO_2$ combining power 65.7 vol. per cent.

A gastrointestinal series revealed obstruction of the small bowel with many grossly dilated loops of jejunum in the left upper quadrant, and there was a large, sharply defined, smooth mass in the right mid-abdomen. Dr. Hampton will discuss the films in greater detail (Figs. 1 and 2).

DR. HAMPTON: I do not think that I can make a diagnosis. There is a mass, larger than a grapefruit on the right side, which displaces the ascending and transverse colon upward, but there is no evidence that it involves the colon. The jejunum is markedly dilated and filled with barium down to the region of the left sacroiliac joint, where it points toward the lower margin of the mass on the right. Superimposed on the mass there are many loops of ileum which are unusually small and the question arises whether these loops are within the mass or whether they are outside and reduced in size from pressure. If they were reduced in size from pressure, they should be flattened and not smaller in all directions as they appear. The most likely explanation for the small size of the ileum is that, because of the almost complete obstruction, only a small amount of barium is reaching the ileum. The ileum is contracted due to its small contents. The psoas muscle on the right is obliterated which is some evidence that the mass is retroperitoneal. In the lateral view the mass is unusually well demonstrated. It has sharp, smooth margins and its center is about 3 cm. anterior to the margins of the vertebrae. The anterior position is evidence against its being retroperitoneal.

FIG. 1

FIG. 2. Lateral view.

Why should the obstruction be on the left side if the visible mass on the right is producing it? I am forced to the conclusion that there is also a tumor present on the left and that the mass visible on the right is not the primary cause of the obstruction. The ileum is contracted due to its small contents rather than because it is involved in the mass or because it lies in a retroperitoneal hernia.

The right kidney is not seen and I cannot exclude the possibility of the mass being a tumor of the kidney. The picture does not suggest tumor of the kidney, however, as the cause of the obstruction. A tumor of the abdomen, which extends into the retroperitoneal space would obliterate the psoas muscle and might produce this picture. This patient is a woman and I would like to accuse the ovaries, but I do not believe ovarian malignancy would produce gastrointestinal bleeding.

Dr. Castleman: A carcinoma of the ovary may so invade the sigmoid as to produce intestinal obstruction and occasionally hemorrhage. I can recall two cases where the ovary and sigmoid were so adherent that we were unable grossly to decide in which the tumor was primary.

Dr. Hampton: My conclusions then, on reviewing the case, are that the patient has small bowel obstruction, the nature of which I am unable to determine. She also has a mass in the right side of the abdomen which may be a tumor of the kidney but which I believe has nothing to do with the intestinal obstruction.

Dr. McPeak: I suggest carcinoma of the kidney

Dr. Hampton: We must consider two tumors.

Dr. Schatzki: At the time of interpretation we were worrying about these two defects within the dilated loops of the small intestine (Fig. 1). They were not routinely visible and therefore discarded them as probably representing small intestinal content. I assumed that the loops of the small intestine overlying the visible mass in the right side of the abdomen were narrowed because they represented intestine beyond the point of obstruction.

Dr. Hampton: We have seen one or two very large small bowel tumors which were not demonstrated in any of the films because the motor meal was either above or below them at each of the hourly examinations. It is still possible that there could be a carcinoma of the small bowel, but I cannot link the large tumor on the right, which appears to be retroperitoneal, with the intestinal obstruction. I would rather believe that there is a carcinoma of the small bowel than a carcinoma of the ovary, and that the mass on the right is a tumor of the kidney.

Dr. Schatzki: I believed the mass on the right side to be fairly definitely retroperitoneal and had difficulty in explaining the intestinal obstruction by such a retroperitoneal mass. I thought it might be a retroperitoneal malignant tumor which might have secondarily involved the gut.

Dr. Holmes: The patient has an obstructing lesion in the small bowel. You located the position and portion of the bowel involved and there was a history of bleeding so that the patient must come to operation. What more could you expect from the examination?

Dr. Schatzki: I was thinking a little on similar lines when I was interpreting these films, but I do not believe that one should be so easily satisfied as that. In a case of obstruction, it is important for the surgeon to know what the obstruction is due to. He should know beforehand, if possible, whether the obstruction is due to inflammation or tumor, and if it is due to tumor, whether it is benign or malignant.

It is not our practice to give barium by mouth to a patient with intestinal obstruction. In this particular instance, the diagnosis of intestinal obstruction was not made clinically, and the gastrointestinal series was started before we were aware that obstruction existed. The patient had a large abdomen which she maintained had always been large as long as she could remember. However, the lesion might have been demonstrated in a satisfactory manner and without danger to the patient by passage of a tube and introduction of barium which could later be withdrawn.

Dr. Rutherford: The patient was referred to the Surgical Service where we arrived at very much the same conclusions that have already been discussed. The most tenable diagnosis seemed to be a large ovarian cyst riding out of the pelvis with malignant degeneration causing secondary metastatic small bowel obstruction. Whatever else, the problem was one of relieving chronic partial small bowel obstruction. Since it seemed to be a procedure requiring several stages, an enterostomy was planned, sidetracking the bowel around the obstruction.

At operation a large retroperitoneal cystic mass was found on the right which was entirely independent of the obstructive process. On the left there was a mass having the appearance of malignancy involving the small bowel and sigmoid. Breaking down the ligament of Treitz a dilated loop of jejunum was identified. A collapsed loop of the distal bowel was also found and a side to side anastomosis was done. Without further attempt to explore, the operation was concluded. The feeling was that the process represented a primary carcinoma of the sigmoid with secondary bowel obstruction and that the mass on the right was a retroperitoneal tumor entirely independent of the process on the left.

Dr. Hampton: Do you think that this small shadow at the upper margin of the large rounded mass is the kidney?

Dr. Schatzki: I thought that the upper smaller shadow probably represented the kidney and said in my report that the large mass seemed to be outside the kidney shadow, but that a pedunculated cyst or tumor of the kidney was a definite possibility.

Dr. Hampton: I cannot believe that the patient had a carcinoma of the sigmoid because the proximal colon is small rather than dilated.

Clinical diagnosis—Small intestinal obstruction. ?Carcinoma of the ovary.

Dr. Hampton's diagnosis—Small intestinal obstruction, cause undetermined. ?Tumor of right kidney.

Pathological diagnosis—Carcinoma of the sigmoid with invasion and obstruction of the jejunum. Benign cortical cyst of the right kidney.

Dr. Castleman: The patient died several days after the operation and, at autopsy, the large mass in the right abdomen proved to be a perfectly benign cortical cyst of the kidney and apparently played no part as the cause of the patient's symptoms. The cyst measured 15 cm. in diameter and was located at the upper pole. There was also another smaller cyst, 6 cm. in diameter at the lower pole.

The small bowel obstruction was quite unusual. Upon opening the abdomen we found loops of small intestine adherent to the colon in the region of the left upper quadrant, possibly more medial than lateral. Further dissection showed that the adherent mass was composed of a loop of jejunum about 10 cm. in length, attached to the upper sigmoid. In attempting to free these loops a round mass of necrotic tumor about 3 cm. in diameter was broken into. The jejunum in this region contained three polypoid tumors, 1 to 2 cm. in diameter, which appeared to extend through the wall into the mass of necrotic tumor adherent to the upper sigmoid. At this point there was an annular constricting, firm, ulcerated apparent carcinoma 2 cm. in length of the colon. At the time of the autopsy we were unable to decide whether the lesion was primary in the colon or in the jejunum with extension into the other, or whether each might be a separate tumor. From the gross appearance of the polyps in the jejunum it did not seem likely that they could have become malignant and produce such a scirrhous lesion in the colon. Histologically all the tumors in both small and large bowel are the same—a well differentiated adenocarcinoma. Our feeling, therefore, is that the tumor was primary in the upper sigmoid, that it extended through its wall forming a mass of necrotic tumor, which in turn invaded the jejunum in three places, produced the polypoid lesions and the obstruction.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Publisher: Charles C Thomas, 220 East Monroe St., Springfield, Illinois.

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich. Office of publication 220 E. Monroe St., Springfield, Ill. Information of interest to all readers will be found on page iv.

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Twenty-fourth Annual Meeting: St. Louis, Mo., 1939.

EDITORIALS

THE ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY*

NECESSITY OF CHANGE IN TIME, PLACE AND PROGRAM

THE Constitution and By-Laws of the American Radium Society provide that the annual meeting be held on the Monday and Tuesday of the week of the annual session of the American Medical Association. Nothing had occurred to disturb this arrangement until this last year when we were requested to consult the Secretary of the American Medical Association before we could obtain the hotel meeting place for our sessions in spite of the fact that arrangements had been made a year previously with one of the best hotels. The Local Committee on Arrangements found plans difficult to make for the 1938 meeting and yet there were many accommodations available.

It must be understood that, when those responsible for the arrangements of the physical factors and the hotel accommodations for the American Medical Association complete these matters, they have a contract with the city, the hotel men's association and the auditorium authorities that gives the American Medical Association absolute control of these accommodations for the week of their meeting. It must also be realized that there are about 35 organizations, some smaller and some larger than the American Radium Society, which seek to have their annual meeting during the same week of the American Medical Association. These meetings are usually held on Monday and Tuesday as are our meetings. They usually have four scientific sessions and a banquet on Monday evening. Some of these societies meet the week before and others on the Friday and Saturday of the week of the sessions of the American Medical Association.

It was formerly true that the American Medical Association opened its meeting on Tuesday evening. Then the Section meetings were held on the three succeeding days, with the usual fraternity and alumni dinners on Wednesday evening; the Presidential Reception was held Thursday evening, after which many went home, although there remained the section meetings for Friday.

Things are different now. The American Medical Association provides excellent general scientific sessions on Monday and Tuesday. The meetings of the various specialty boards of certification hold their examinations the previous week and on Monday and Tuesday. These boards require hotel accommodations that are exacting, and the accumulation of small society meetings becomes a disturbing element. The House of Delegates of the American Medical Association holds meetings on Monday and Tuesday and their reference committees also demand the attention of many of the leaders of these various smaller societies. The function of those versed in radiologic thought and action was exemplified by the results obtained from resolutions that were presented and received favorable action at the 1938 meeting.

And speaking of resolutions, it may be well to quote the resolutions from the reference Committee of the House of Delegates of the American Medical Association concerning this proposition of the independent organizations. The Reference Committee on Sections and Section Work had the following paragraph in their report:

* Presidential Remarks at the Annual Banquet of the Twenty-third Annual Meeting of the American Radium Society, San Francisco, Calif., June 13–14, 1938.

The report of the Council on Scientific Assembly has been reviewed and your reference committee particularly commends the suggestion of the Council that scientific sections of the Association may combine their sessions when the subjects presented are of mutual interest. To further the attendance at the general scientific meetings and sectional programs, your reference committee would be happy to endorse any activity of the Council on Scientific Assembly that would discourage independent societies from holding their meetings during the sessions of the American Medical Association.*

Another resolution reflecting upon this subject was reported by the Reference Committee on Miscellaneous Business as follows:

2. Resolutions on Services of Section Delegates: Your reference committee was fortunate in having some of the section delegates meet with it for consideration of this resolution.

This petition is based on the following facts: 1. The existence of numerous societies of specialists wholly independent of the American Medical Association. 2. Occurrence of discussions and procedures in those societies which sometimes indicate a lack of understanding of the policies and procedures of this House. 3. A desire by sponsors of this resolution to correct these misunderstandings and substitute intelligent cooperation therefor.

Your committee is in complete accord with the desirable objectives of these resolutions and offers the following recommendations:

(*a*) That this House request delegates from the several sections to act as liaison between the House and those special societies whose scientific interests are included in the respective scientific sections of the American Medical Association which the delegates represent.

(*b*) That the Secretary of the House shall each year communicate with presidents and secretaries of all such societies as his judgment may dictate, for the purpose of identifying section delegates and reaffirming to these societies the desire of the American Medical Association for sympathetic cooperation in coordinating all medical interests and activities.

(*c*) That the Secretary of this House shall after each annual session communicate with the delegates from each section advising them regarding the desire of the House in this respect.†

* *J. Am. M. Ass.*, July 2, 1938, *111*, 56.
† *J. Am. M. Ass.*, July 2, 1938, *111*, 60.

The above resolutions will indicate that the situation under discussion has been of definite concern to those upon whom the successful issue of the annual meetings of the American Medical Association rests as a responsibility.

There are those members of the independent societies who strongly contend that by holding their own meetings at the same time and at the same place as the annual meeting of the American Medical Association their attendance is increased. The actual facts develop that this argument is questionable. The attendance at the section meetings has suffered from the decision of many specialists to attend their special society during the preceding week or the first two days of the week and then go home and forget the section meetings of their specialty. This detracts from the interest of the extra-specialty physician who expects to hear the leaders take part in discussions and present papers. The tendency of special societies to fix their annual meetings in direct conflict with the meetings of scientific work of the American Medical Association will, if matters get much worse, find the American Medical Association in the position of playing second fiddle. It is obvious that this is just as much a matter of concern for these societies as for the American Medical Association.

Another point of discussion hinges upon whether it is good or bad policy to find the major stress upon a program of specialty interest, such as radium therapy, within a small group of members or whether it would not serve a more useful purpose to have such papers distributed throughout the general sessions and the section meetings of the American Medical Association. Would not the gospel of better radium therapy be spread more widely if its messages were heard by general practitioners and physicians from other specialties? Could arrangements be made to have one session of the Section of Radiology taken up with radium topics and perhaps a good essay upon radium therapy in the Monday or Tuesday general sessions?

The membership of the American Radium Society is not composed of radium therapists alone. There are among its members pathologists, physicists, surgeons, executives of cancer institutions and research workers in the cancer field. The member who practices radium therapy alone is rare. The majority are within the field of cancer therapy.

In view of the impositions of the Constitution and By-Laws of the American Radium Society, any change in meeting place and time demands a change in these instruments. Various solutions may be enumerated. No one solution seems to be evident because of the varied interests of the membership. As a basis of discussion the following suggestions are offered:

1. Combine the annual meeting of the American Radium Society with the meeting of the American Roentgen Ray Society after negotiations that would provide ample program space for papers on radium therapy with those on roentgen therapy. These societies now cooperate in the publication of an excellent Journal.

2. Combine the annual meeting of the American Radium Society with the Radiological Society of North America on the same basis.

3. Combine the annual meeting of the American Radium Society with the American College of Surgeons rather than the American College of Physicians, because radium therapy is essentially a surgical procedure.

4. Combine the annual meeting of the American Radium Society with the American Association for the Advancement of Science which meets each year during Christmas week, because this organization has a medical section and lately has developed programs on cancer that touch intimately the problems of radium therapy. This organization seems to have many units which hold their annual meetings during this larger combined Association meeting.

5. Plan the annual meeting of the American Radium Society at another period of the year and independent of any other organization. It may now be the time to try out a different type of annual meeting, using centers of radium and cancer interest with more stress upon the clinical advantages of a meeting place. Up to the present we have never used other than the essay type of meeting. It has been suggested that if we are not to meet at the time of the American Medical Association, there is a necessity to offer members more than the mere reading of papers which can be found later in this JOURNAL, and that the meetings should combine an opportunity to observe the work of some of our members and the setups in institutions. It has also been suggested that the Janeway Lecturer be obtained from without the ranks of our Society and a traveling honorarium provided therefor.

6. There is the suggestion that the annual meeting be enlarged to provide an intensive program of one week upon practical and theoretical radium therapy, using the evenings for scientific program material and utilizing all of the advantages of different centers, both clinical and physical. Such programs would attract other than members, who would pay registration fees to defray the expenses of such meetings, with classes of instruction given by outstanding authorities. There are at least five centers in America that could provide a proper setting for such an experiment.

7. Negotiations could be undertaken to continue our annual meetings at the time of the American Medical Association but upon a basis that would offer no interference with the Association.

The membership of the American Radium Society is about 175. About seventy-five of this number attend the annual meeting. There has never been any drive for membership.

These are questions that confront our Society and the Executive Committee. What is your pleasure?

EDWARD H. SKINNER

THE HENRY HARRINGTON JANEWAY LECTURE AND MEDAL

EACH year at the annual meeting of the American Radium Society is given the lecture by some outstanding and appropriate individual in honor of a pioneer American radium therapist, Dr. Henry Harrington Janeway.

A medal has been struck and a replica is presented to each one who is honored upon this annual occasion. The essayists and recipients of the Janeway Medal have been the following:

Dr. James Ewing	1933
Dr. Francis Carter Wood	1934
Dr. George E. Pfahler	1935
Dr. Curtis F. Burnam	1936
Dr. Douglas Quick	1937
Dr. Henry Schmitz	1938

The medal was designed by Miss Stephanie Prince of Kansas City, Missouri and executed by Tiffany of New York. The subject chosen is from Norse mythology and it symbolizes the sacrifice made by those who have worked with radium.

The legend of Odin seems appropriate because he sacrificed an eye in search of wisdom and he was said to have power over the precious minerals buried in the earth. The legend is that Odin, the ruler of the gods, having wandered over the earth in search of knowledge, finally came to Mimir's well in whose waters wisdom and wit lay buried. But the price asked for a drink, from the well was Odin's right eye. So Odin plucked out his eye and gave it to Mimir.

Concerning Odin's power over metals, the legend relates that "he understood the songs by which the earth, the hills and the stones and the sounds were opened to him and he bound those that were in them by the power of his word and he went in and took what he pleased."

The reverse of the medal carries the images of Odin's two ravens, Hugin, endowed with thought and reflection, and Munin, endowed with memory. These two ravens left the shoulders of Odin and flew each day in search of news and each night returned to relate what they had found.

It does not take much flight of the imagination to translate the significance of these mythological items into the ken of radium lore. The sacrifice of those who pursued the study and application of radium is glorified. The ambitions of the student to find out all that goes on in the world and appropriate such knowledge is represented in the searching ravens. The symbolism of the medal seems complete.

Medals are metallic memory, says Bland-Sutton in his "Story of a Surgeon" that Rudyard Kipling prompted him to write. While imaginative and inspiring in design, they are only pieces of metal of no use in currency and struck to commemorate an event or an individual. Most of the medical medals of England are of gold and are supposed to be worth about fifty pounds, sterling. But when an attempt is made to dispose of them, the goldsmith always saws it in two because the core is usually of lead and only the surface is of gold. Many eminent recipients have sought to sell their medals only to find them gilded baubles.

This recalls Dryden's satirical lines on medals:

"Golden to the sight,
So base within, so counterfeit and light."

Bland-Sutton preaches pertinently to medalists when he reminds them that there have always been other contestants for the same honor and it is good to realize that there are others just as clever. This helps to rub off the mental asperities and saves them from conceit. Medals are milestones in the history of institutions that are not given for ostentation but for remembrance and reward. They bring to mind the names of great men who laid the foundations of advantages which present and future generations may enjoy and which it is the duty of followers to extend.

While the Janeway Lecture had been a regular feature of the annual banquet of the American Radium Society for several years, it was not until 1937 that the medal

Norse Mythology tells us that the god, Odin, who was said to have power over the precious minerals buried in the earth, wandered over the earth in the search for knowledge. Finally Odin came to Mimir's well, in whose waters wisdom and wit lay buried. The price Mimir asked for a drink from his well was Odin's right eye. So Odin plucked out his eye and gave it to Mimir for a potion of wisdom.

Odin possessed two ravens, Hugin (thought or reflection) and Munin (memory or remembrance). These ravens perched upon his shoulders. To them he owed a great part of his wisdom for each day they flew forth through the expanses of the universe returning to teli him of all they had seen and reported upon the events and progress of the world.

was struck. At the evening meeting devoted to the American Radium Society during the sessions of the Fifth International Congress of Radiology, all of the Janeway Lecturers from 1933 to 1937 were present upon the platform and received their inscribed medal with the following remarks:

Dr. James Ewing. To one who has served to provide the pathways of pathological knowledge of tumors; who has produced a textbook that serves as a pathological bible for research workers and clinicians alike; who has served the most useful purpose of establishing radiation values in tumor therapy; who has directed a specialized hospital for cancer therapy that has become a model; who has conducted the clinical material of this cancer hospital in such a manner that it has become a mecca for those seeking knowledge in cancer therapy; who has given such support to the staff that there has been cooperation without the sacrifice of individual enterprise or development, and who has been sensible in his prophecies and lenient in his criticisms and tolerant to personalities; who was the first Janeway Lecturer of 1933; to you, Dr. James Ewing, the American Radium Society presents this medal in honor of that occasion.

Dr. Francis Carter Wood. To one who organized, built and directed the first cancer research institution in America, the Crocker Institute for Cancer Research of the Columbia University; who has conducted experimental mouse tumor studies upon tumor metastasis, tumor biopsy and tumor irritants; who has proved the usefulness of *Drosophila* as units of biological study of radiation dosage; who has edited a leading cancer journal; who has been a leader in cancer control, prevention, publicity and roentgen radiation therapy; who has maintained an honesty of mind, exhibited rare self-restraint in his attitude toward misguided cancer enthusiasts, and who has forged new pathways for the research study and control of cancer; to you, Dr. Francis Carter Wood, the American Radium Society awards this metallic memento for the second Janeway Lecture of 1934.

Dr. George E. Pfahler. To one who has been a leader in roentgen diagnosis and radiation therapy over a period of thirty-five years; who is the cordial and beloved Dean of American radiology; who has produced constantly useful and numerous articles upon roentgen protection, saturation dosage and protracted therapy; who has given liberally of his time and energy in promoting ethical consultative radiology among his colleagues; who has served usefully in the development of this and all previous International Congresses of Radiology; who has endeared himself to all of us by his sympathy, understanding, tolerance and faithfulness; to you, Dr. George E. Pfahler, the American Radium Society presents this Janeway Memorial Medal for the 1935 Lecture.

Dr. Curtis F. Burnam. To one who has labored in the field of radium therapy since the earliest clinical years; who has assisted in the introduction and establishment of radium merits in treatment; who provided the earliest tables of radium dosage; who constantly demanded the clinical unity of diagnosis and therapy; who has established the radiotherapeutic department of one of America's leading medical schools and hospitals, and who has generously, benignantly and smilingly served to develop the prestige of radium therapy in America; to you, Dr. Curtis F. Burnam, the American Radium Society conveys this disc of bronze to commemorate the 1936 Janeway Lecture.

Dr. Douglas Quick. And to you, assistant and colleague of Janeway; the constant friend of ambitious students; the indulgent observer of a changing world, who has mastered radium therapy without sacrifice of equilibrium, temper or deportment; who has endeared himself to his chosen colleagues by faithful devotion to their advancement; who has cherished his enemies to their everlasting discomfiture; who has linked radium therapy to surgical procedure; upon you, My Good Canadian Friend, this heavy bronze is bestowed with the best wishes of the American Radium Society.

The 1938 Janeway Medal was awarded to Dr. Henry Schmitz at the meeting in San Francisco. Dr. Henry Schmitz is a worthy recipient and is recognized for his contributions to the development of radium therapy, more particularly in the field of carcinoma of the uterus. He is a charter member of the American Radium Society, constantly serving upon committees, contributing to the program and discussions with characteristic emphasis and finality. He was President of the Society in 1921. He has represented the American Radium Society upon the American Board of Radiology since its establishment and was returned to succeed himself for another term of service to American radiology.

Edward H. Skinner

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Chicago, Ill., 1939.

American College of Radiology
Secretary, Dr. E. L. Jenkinson, 1439 S. Michigan Ave., Chicago, Ill. Annual meeting, 1939: To be announced.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: St. Louis, Mo., 1939.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Pittsburgh, Pa., Nov. 27–Dec. 2, 1938.

Radiological Section, Baltimore City Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Special meetings may be called by the Chairman.

Radiological Section, Los Angeles Co. Med. Soc.
Secretary, Dr. M. L. Pindell, 678 S. Ferris Ave., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. Harry Hauser, 3395 Scranton Rd. Meetings are held at 6:30 P.M. at the Mid-Day Club rooms on the fourth Monday of each month from October to April, inclusive.

Denver Radiological Club
Secretary, Dr. E. A. Schmidt, 4200 E. 9th Ave., Denver, Colo. Meets third Tuesday of each month.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida State Radiological Society
Secretary, Dr. J. H. Lucinian, 403 Huntington Bldg., Miami, Florida. Meetings held twice a year, May and November.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets twice annually: in November and at annual meeting of Medical Association of Georgia in the spring.

Illinois Radiological Society
Secretary, Dr. E. P. Halley, Decatur and Macon County Hospital, Decatur, Ill. Meetings held quarterly, time and place designated by president.

Indiana Roentgen Society
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

Long Island Radiological Society
Secretary, Dr. S. G. Schenck, 115 Eastern Parkway, Brooklyn, N. Y. Meets at Kings County Med. Soc. Bldg. on fourth Thursday, each month, October to May, 8:30 P.M.

Michigan Association of Roentgenologists
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

Minnesota Radiological Society
Secretary, Dr. H. M. Weber, Mayo Clinic, Rochester, Minn.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. W. J. Marquis, 198 Clinton Ave, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

New York Roentgen Society
Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

Pacific Roentgen Club
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Annual meeting, May, 1939. Exact time and place to be decided.

Philadelphia Roentgen Ray Society
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St

Pittsburgh Roentgen Society
Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St., Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Fran-

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

cisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston. Meets at time and place of South Carolina Medical Assn.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. G. D. Carlson, 3121 Bryan St., Dallas, Texas. Next regular meeting in San Antonio, Oct. 22, 1938.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgensellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson, Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

REPORT OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY*

The Inter-Society Committee for Radiology was created to provide a national headquarters for all American radiology. Its function is to collect facts and information, to make this information available to members and local groups, and to offer advice and counsel when requested. Through this national office of American radiology, organized radiology is able to present its case to the American Medical Association and the American Hospital Association, and other national agencies. Likewise it is able to keep in touch with the activities of these agencies, to evaluate their effects upon radiology and to interpret trends as they bear upon the welfare and progress of radiology.

There are several particular items of successful activity upon the part of the Committee as a whole, of the Executive Secretary as a fountain of factual and analytical information, and of the earnest and sincere work of the individual faculties inherent in the members of this Committee, that will be detailed later.

The Inter-Society Committee wishes to acknowledge the splendid help that it has received from many individuals who have rallied to the support of our program in various situations and localities. The Committee acknowledges the importance of the radiologists chosen from each state as a human liaison with the problems of each state. Confidential and reliable information has helped the Committee to avoid errors of judgment and permitted us to form opinions and make decisions that have stood the test of the resulting experience.

The Advisory Committee, composed of the secretary and chairman of the executive council of each of the supporting societies, has aided materially in the determination of policies and has helped the Committee to develop a confidence in the merit of the program as it develops.

* Presented by E. H. Skinner, M.D., before the Thirty-ninth Annual Meeting of the American Roentgen Ray Society, Atlantic City, N. J., Sept. 20–23, 1938.

The Committee has sent the Executive Secretary to a number of cities where local radiologists have asked for help in excluding their services from hospital schemes of insurance and we are glad to report that these efforts have been successful in nearly every instance. We are not conscious of any complete defeat. We do know of innumerable victories. Details of such activities can be obtained from the Executive Secretary. They are too voluminous for this report.

At every opportunity we have urged and encouraged radiologists to improve their hospital arrangements. The Committee cannot force an individual hospital to revise an unfair contract with its radiologist but it can influence the local situations by calling attention to the resolutions of the Councils and House of Delegates of the American Medical Association that defend our ambitions to avoid the exploitation of radiological practice. The only pressure that organized medicine has at its disposal in defeating unfair practices and tactics by hospitals is through the approval listing of hospitals, internships and residencies by the Council on Medical Education and Hospitals of the American Medical Association.

The Committee feels that real progress has been made in cementing the problems of radiology into the whole picture of the American medical profession. The healthy attitude of the House of Delegates and the splendid cooperation of the various Councils and the favorable action of the Board of Trustees and the national secretary, Dr. Olin West, are indications of the usefulness of this Committee to radiology. The actual facts of the proceedings at the San Francisco meeting of the American Medical Association have been printed in both the national journals. The *Journal of the American Medical Association* made these resolutions a matter of editorial comment.

The Committee has prepared, and this only through the capable Executive Secretary, two important documents for publication in the national journals. One is based upon "The Modern Hospital and Its

Relations to the Practice of Medicine."* This is factual and carries citations to support the contentions. The ever-increasing activity of the hospitals and their national organizations and publications to establish medical practice by hospitals makes this an important contribution in support of our demand that radiology continue as medical and not hospital practice. The other article is titled, "What is the Issue?"† This is a more timely exposition of the most recent editorial opinion of hospital enthusiasts and furnishes the radiologists with ammunition and argument to controvert the specious claims of omni-service by hospitals. We direct your attention to these two items. They are to be followed by others. We would like to feel that the membership would support our requests for prompt printing of such informative articles by the journals controlled by our societies. We would not wish to sacrifice the most important scientific contributions but we do feel that the present stress and strain of the times warrants some stress upon the economic factors of radiological practice. We believe that members want these items. We would cordially invite an expression from the membership upon this point.

The Committee wishes to acknowledge the help and the cordial cooperation of various executive committeemen from the several societies in the development of standards of radiological practice. Such standards must be erected for the benefit of the Council on Medical Education and Hospitals if it is to carry out the instructions of the 1938 House of Delegates by imposing restrictions to influence hospitals that persist in exploiting any type of medical practice. This is a long time problem and its solution seems to depend at this time upon the solidarity of the American Medical Association. If the influence of this parent organization is weakened or dissipated, our problems will be multiplied and perhaps stultified.

This report could be expanded into a volume if it attempted to detail the various and sundry activities of the committeemen and the Executive Secretary. This seems absolutely uncalled for and if any individual member wishes specific information, the Executive Secretary and the Committee will be only too glad to make the effort to completely satisfy that member. It now seems expedient to pass from the practical exposition of performance to the dreams and implications of the future.

The Committee believes that the following items represent the problems that threaten the welfare of the medical profession and radiological practice:

1. The attitudes and practices of hospitals and the organized hospital world which tend to place radiology under the domination of a lay board of trustees, establishing it as a technical service to be rendered by hospitals instead of a professional service to be rendered by private physicians.

2. The attempts to define radiology as a hospital service by including it among the hospital benefits offered in group insurance plans.

3. The tendency for some hospitals to look upon the department of radiology as a legitimate source of revenue to pay losses sustained in other departments, thus depriving the radiologic department of a portion of its legitimate income.

4. The attempts to dismember radiology and consequently destroy the specialty by dividing it into technical and professional stages.

5. The increase in group and cooperative laboratories which supplant established and trained radiologists engaging in private practice.

6. The threat of competition by the state through free diagnosis and treatment of cancer, and general diagnostic centers, thereby discouraging private enterprise and individual initiative by radiologists.

Let it be emphasized here that when the Committee approaches problems in medical economics it is not primarily concerned with the fact that some new development may curtail the income of an individual practitioner. It is concerned with the fact that these developments may injure the

* Am. J. Roentgenol. & Rad. Therapy, August, 1938, *40*, 295.
† *Ibid.*, Sept., 1938, *40*, 439.

growth of radiology, decrease the quality of the service to be offered to patients, and discourage the attraction of competent new matriculates to the field.

In appraising those problems which concern every practicing radiologist it becomes necessary to first assemble some facts and evaluate some trends. The analysis of these facts and trends has occupied a large portion of the time of the Committee and its Secretary, Mr. Cahal, during this first year of its existence. To obtain facts we have distributed a questionnaire to the 1,500 members composing the four parent societies. The tabulation of the nearly 1,000 returns received represents a big task and, even with the help of the statistical department of the American Medical Association, we are not yet in a position to present to you at this time the results of this study. The full report will be published within a short time. Also in pursuit of facts we have distributed numerous inquiries to our mailing list of state representatives. In addition we have carefully studied all factual reports issued by other official bodies in the medical, hospital, and political field in search of information that will help us to accurately measure the status and the problems of radiology.

To properly evaluate trends and thus chart a proper course of action for the future we have maintained a close association with the American Medical Association, the American Hospital Association, and other such agencies for the purpose of observing actions relating to radiology and insofar as possible of assisting in the guidance of those actions. In anticipation of a federal sickness insurance program, which the most sanguine conservative must admit is a foregone certainty, we are making every effort to predict and to help establish the position of the radiologist in medical practice when and if such a program is instituted.

All these facts, in the form of bulletins, journals, reprints, and statistical surveys are being collected, indexed, and filed in our headquarters office. In the meantime we have established a focal point of contact between all organized radiology and the national associations representing other specialties, organized hospitals, and the American Medical Association. Illustrative of the value of such association is the splendid report issued April 30, 1938, in the *Journal of the American Medical Association*, by the Board of Trustees of the American Medical Association, previous to the San Francisco session of the House of Delegates and which set the stage for the encouraging stand taken by the American Medical Association during the meeting on behalf of radiology. The Committee, through its Secretary, was given the privilege of supplying information to assist in the preparation of that report. Its approval by the House of Delegates marked a decisive victory in the fight by radiologists to maintain their specialty against threats of domination and exploitation by the lay boards of trustees of hospitals. Its influence will be felt in the determination of developments for a long time to come.

The chief problem confronting the Committee during the past year has been in connection with hospital insurance. Here arose a question of supreme importance to the science and practice of radiology. Was radiology a technical service to be offered by incorporated hospitals as a part of hospital care on an annual premium basis, or was it a medical service to be provided by private physicians on a fee-for-service basis like other medical procedures? To repeated demands by this Committee and by the American Medical Association that medical services be excluded from hospital insurance schemes, the American Hospital Association took an acrimonious stand and insisted that radiology was a part of hospital care and must be included as a part of hospital benefits in all such plans. Month after month their official journal has advanced principles to justify their contention that radiology is a service of, by, and for hospitals and as such must be included in the insurance plans.

While the record in combating this dangerous development is by no means perfect we are pleased to report that a successful defense has been waged. Several

of the largest plans in existence today include radiology as a hospital service, but in the thirty or more plans adopted throughout the country during the past year only one or two have, to our knowledge, included radiology. The American Medical Association has taken a firm stand in support of the radiologist, the pathologist, the anesthetist and others who object to a new development in hospital economics that will result in their specialty being taken over by the hospital. Throughout the past year the battle raged in Philadelphia between an adamant hospital council and a determined group of local radiologists and only within the past month were Philadelphia radiologists able to win their point. The Committee's Secretary spent much time in Philadelphia in assisting the local roentgen society. His services have been useful in similar controversies in Denver, Kansas City, Michigan, Florida and other localities where radiologists appealed for help in protecting their specialty against fundamental injury through the institution of hospital insurance schemes. At present he is working with our members in Baltimore in an effort to obtain a correction of that plan and it is hoped that local groups in other communities who were forced to accept the wrong kind of a plan will take up the battle and, backed by the full support of the American Medical Association, insist upon a revision that will leave their profession in the same position as other medical specialties. The credit for correction of the plans in California which originally included radiology belongs to a militant group in the Pacific Roentgen Society. These members have demonstrated what a positive program will do. The Inter-Society Committee for Radiology could accomplish a great deal more if there were more of this type of aggressive local group in all parts of the country.

The Secretary of the Committee, Mr. Cahal, has carried out his duties under the close supervision of the members of the Committee. While a large part of his time has been spent in traveling to various cities at the request of local roentgen groups it has been necessary for him to dispose of a large amount of work through the headquarters office. In addition to routine details and frequent conferences with councils of the American Medical Association and other agencies with headquarters in Chicago, daily inquiries are received at our office from hospitals, medical societies, member radiologists, and social agencies calling for study and reply. Any such inquiry which involves a question of policy is referred to members of the Committee before action, and if of sufficient importance it is in turn referred to our Advisory Committee, composed of the secretaries and chairmen of executive committees of the four participating societies.

During the past year the Secretary has made one or more trips to the following places, either to attend a meeting or offer assistance: Philadelphia, New York, Pittsburgh, Boston, Washington, Baltimore, Atlantic City, Denver, Los Angeles, San Diego, San Francisco. He has sat in conferences with medical society councils and addressed medical societies in Michigan, Illinois, Indiana, Missouri, Pennsylvania, and Colorado. Soon after starting his duties he visited Detroit, Cleveland, and other localities which offered convenient stopping places on other official trips. Next month he will visit Texas for a meeting with the state radiological society.

The editors of both this Journal and of *Radiology* have generously agreed to set aside a regular department for monthly reports and articles by or sponsored by the Committee. This we feel is a more desirable and a less expensive way of keeping in contact with the members than by publishing a bulletin of our own. Through these regular reports we hope to keep every member thoroughly aware of important developments and maintain a concerted opinion among the members of our own profession.

If it is to be properly represented in the profound changes taking place in the social and economic phases of medical practice, the profession of radiology must be thoroughly awake, strongly unified, and aggressively articulate. We feel that radiologists have these three things in the program of the Inter-Society Committee for Radiology.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Henry, C. Bowdler. Cysts of the nasopalatine canal. *Lancet*, June 5, 1937, *1*, 1326–1327.

These cysts, also known as medium anterior maxillary cysts, occur in about 1 per cent of the population. In their simplest form, they appear in the bone above and below the incisor teeth. The outline of the cavity is well defined, the wall consisting of loose connective tissue lined with epithelium.

As a rule, nasopalatine cysts are asymptomatic. When large, attention may be called to their presence by swelling on the hard palate or deep to the attachment of the frenum labii. Though painless, smooth, and hard, they may erode and fluctuate. Fistulous tracts sometimes develop and produce pain when blocked. As a rule, the pain radiates into the glabella or maxilla.

Radical operative removal is the treatment of choice though drainage alone sometimes suffices.—*P. J. Hodes.*

Northfield, D. W. C., and Russell, Dorothy S. The fate of thorium dioxide (thorotrast) in cerebral arteriography. *Lancet*, Feb. 13, 1937, *1*, 377–381.

The authors present their histological findings in 4 patients in whom they obtained evidence of the retention of thorotrast in the brain following cerebral arteriography. Thorotrast was identified in the lumen or walls of the small cerebral vessels and in the perivascular macrophages.

In view of these findings and because the injections were followed by an aggravation of clinical symptoms in 2 of their patients, the authors considered the use of thorotrast inadvisable unless other diagnostic methods failed.—*P. J. Hodes.*

NECK AND CHEST

Gordon-Taylor, G., and Handley, R. S. An unusual case of hyperparathyroidism anterior mediastinal parathyroid tumour removed by trans-sternal approach. *Brit. J. Surg.*, July, 1937, *25*, 6–16.

The authors report the findings in a patient operated upon successfully for an intrathoracic parathyroid tumor after an exploratory operation of the neck had been negative. There were no secondary manifestations, clinical or roentgenographic, to suggest the presence of the 4-gram retrosternal tumor found at operation. The author believes that all patients with overwhelming evidence of parathyroidism who present no evidence of an adenoma in the neck should be given the possible benefits of a thoracic operation.

The embryology of the neck glands is discussed and evidence explaining the presence of intrathoracic parathyroids discussed. This report contains numerous excellent illustrations which enhance its value.—*P. J. Hodes.*

Haas, Alfred. Observations on malignant disease of the thyroid gland. *Lancet*, May 15, 1937, *1*, 1155–1159.

Reference is made to the various types of thyroid cancer and a few salient clinical observations concerning each type are reviewed. The major portion of the paper pertains to the malignant adenomas of the thyroid.

To look at, these tumors are very much like adrenal glands appearing in isolated nobs in the middle of the thyroid. Grossly, they form hard isolated nodules in normal or adenomatous tissue.

The author calls attention to bone lesions which are sometimes associated with malignant thyroid adenomas. When the bone lesions are removed surgically, they present no evidence of malignancy and have the histological characteristics of benign thyroid tissue. The origin of these bone metastases is problematical. Some believe that goitrous tissue may accidentally enter into the veins and thus be disseminated.

Removal of the tumor and its capsule, when followed by postoperative irradiation, usually results in a cure. The author presents the case records of several patients with these bone metastases and their histological sections which add to the value of the paper.—*P. J. Hodes.*

Finland, Maxwell, and Loverud, Harold I. L. Massive atelectatic collapse of the lung

complicating pneumococcus pneumonia. *Ann. Int. Med.*, June, 1937, *10*, 1828–1847.

There have been a number of reports of atelectasis complicating pneumonias in children and infants but rarely has there been mention of such complication of lobar pneumonias in adults. However, it was recognized roentgenologically in 62 cases of primary pneumococcus lobar pneumonia in adults who were studied at the Boston City Hospital, during the past seven years and in 47 cases of various types of pneumococcus pneumonia which came to necropsy, during the same period.

Rommelaere recognized these cases by physical signs; he distinguished them from pleural effusions by the greater deviation in the position of the cardiac impulse in the latter and the failure to obtain fluid by needle aspiration, in the former. He emphasized the relationship of mucoid sputum. Wm. Pasteur had noted this complication in cases of diphtheria and believed that the explanation was a toxic paralysis of the diaphragm; in postoperative cases he believed there was a reflex inhibition of diaphragmatic movement. In 10 of the 11 cases reported by Thoenes, the right lung was involved and of these the upper lobe, most frequently. However, 5 of 8 of the cases reported by Wallgren showed left-sided involvement. Secondary bronchiectasis has been reported. Thick tenacious sputum was usually associated. Bronchoscopy has been recommended by some; respiratory stimulation with the use of carbon dioxide, by others.

The authors emphasize the clinical aspects of these cases: the patient apparently in the stage of resolution convalescing from lobar pneumonia; sudden seizure of intense dyspnea of short duration after which pleuritic pain, moderate fever and leukocytosis recur; physical signs changing from those of fluid to those of solidification. They stress the importance of noting, repeatedly, the position of the heart, the trachea and the diaphragm.—*A. A. de Lorimier.*

Sayers, R. R., and Jones, R. R. The etiology of silicosis. *Radiology*, March, 1938, *30*, 297–308.

The authors have given an excellent survey of the cause of silicosis. Those interested in the subject should read the entire article which is written so concisely that it is very difficult to abstract.

A list of occupations is given in which silicosis is a hazard. The rapidity of the development of this disease depends upon (1) the concentration of the silica particles in the air and (2) the size of the particle. The greatest harm is done by particles between 1 and 3 microns in size. The authors feel that individual susceptibility has little if any bearing upon the development of the condition. Seventy-five per cent of patients with pulmonary fibrosis caused by silica develop tuberculosis, and some authors go so far as to contend that all nodulation in silicosis is due to superimposed tuberculous infection. This pathological lesion is always progressive even if the exposure to silica is stopped. —*J. H. Harris.*

Thomas, R. W., and Cummins, S. Lyle. Acute silicosis in lead-miners. *Lancet*, Dec. 25, 1937, *2*, 1481–1484.

The particular interest in the patients reported in this article lies in the intensity of the dust hazard and in the rapidity of the development of silicosis and of its fatal termination. The cases occurred in dry pneumatic drilling through hard quartzite rock high in silica. There was no means to control the dust hazard and consequently the miners were exposed to high silica dust concentrations. As a result of numerous deaths, 5 miners still able to work were carefully studied. These patients were taken ill within a short time of each other. The average exposure in these patients was thirty-one months. Death followed on an average of eighteen months after they stopped work. Dyspnea was the most prominent symptom. There was no roentgen evidence of definite nodulation present in these patients. Tuberculosis was found following death in 2 patients; in the other patients, tuberculosis was not identified. The short period of exposure and the fulminating character of the pulmonary changes resembles the changes usually described in the abrasive soap industry and in sand blasters.—*P. J. Hodes.*

Weib, F. H. Grenzen röntgenologischer Differentialdiagnostik bei hämatogen entstandenen Lungenerkrankungen. (Limits of roentgen differential diagnosis in hematogenous pulmonary disease.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1938, *57*, 92–98.

The author reports a number of cases with illustrations showing the difficulty if not im-

possibility of distinguishing a miliary carcinomatosis from a miliary tuberculosis from the roentgen examination of the lung fields. In one case, the autopsy revealed that both conditions were present.—*W. A. Evans, Jr.*

Ellinger, Erika. Paraffinölschädigung der Lunge. (Pulmonary damage due to paraffin oil.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1938, *57*, 84–92.

Six cases are reported, with autopsy findings in 2, showing the pulmonary changes produced by aspiration of mineral oil as seen in the roentgenogram. In view of the serious irreversible character of the lesions, the author warns against the use of intranasal and intratracheal instillation of medicated oils, particularly in children, but also in adults. The oil in the lungs cannot be saponified and acts as a foreign body producing a chronic pneumonia leading to contraction of the lung, pleural thickening, and bronchiectasis in the lower portions of both lung fields. The author's 6 patients were adults, all having had tracheotomies followed by the instillation of oil in the tracheotomy tube.—*W. A. Evans, Jr.*

Contratto, A. W., and Levine, Samuel A. Aortic stenosis with special reference to angina pectoris and syncope. *Ann. Int. Med.*, May, 1937, *10*, 1636–1653.

A systolic murmur over the aortic area plus any other confirmatory evidence substantiated a diagnosis of aortic stenosis, twenty years ago. This was then a common diagnosis but it was found to be too common right after the war and many of the cases which were first considered to have aortic stenosis were later accounted for on the basis of neurocirculatory asthenia.

This study concerns 180 cases in which there were definite criteria for the diagnosis of aortic stenosis: a systolic thrill at the base of the heart; roentgenoscopic visualization of calcification in the aortic valve, and the post-mortem findings. No cases were included in which there were complications in the way of mitral or other endocardial lesions.

There was not a single instance where syphilis appeared to be the cause even though it so oftentimes is responsible for aortic insufficiency and aortitis. Calcification of the aortic cusps was found so frequently that sclerosis *per se* might seem to be a predominant factor. Rheumatic fever or chorea had been associated in 31.7 per cent. The interval between the first infection of this sort and the time when the patient was first examined for a cardiac condition averaged 23.3 years for the females and 28.9 years for the males. The probable relationship of rheumatic fever would be increased to an incidence of 44.4 per cent with the inclusion of more questionable backgrounds: "previous rheumatism, sciatica, growing pains, nosebleeds, etc." (a close comparison with the study by Willius who found a history of rheumatic fever in 46 per cent of 96 cases of aortic stenosis). The age distribution ranged from 13 to 81, though the average was 52.5 years; 60 per cent were males; 40 per cent, females. Systolic blood pressures varied from 80 to 260 mm.; diastolics, from 10 mm. to 156 mm. For males, the average was 138 mm., systolic and 79 mm. diastolic; for females, 153 mm. and 81 mm., respectively. Even though such a range of blood pressures was found it appeared that aortic insufficiencies and arteriosclerosis accounted for most of those which showed a high systolic and that otherwise these cases tended to show a relatively low systolic and slightly elevated diastolic, thereby resulting in a small pulse pressure. Most cases showed cardiac hypertrophy with roentgenographic visualization of enlargement of the cardiac silhouette and the post-mortem findings; the average weight was 669 grams as compared with the average weight of 474 grams for cases of purely mitral stenosis. The most constant physical finding was a loud systolic murmur best heard over the sternal region of the right second interspace and over the midsternum. Characteristically, this murmur was very harsh but similar murmurs have been noted in hypertension *per se*, congenital heart disease, anemia and hyperthyroidism. The finding of a systolic thrill, especially if congenital heart disease could be ruled out, was most diagnostic, but it was noted in less than half of the cases. Usually, the rhythm was regular and the pulse rate tended to be slow. Fourteen of the 180 cases showed defects in conduction as manifested by electrocardiographic evidence.

The configuration of the heart, as studied roentgenologically, was usually boot-shaped—as was to be expected in cases of hypertrophy of the left ventricle, but as seen also in cases of aortic insufficiency *per se*, and in some cases of hypertension. Thirty-two of these cases were studied roentgenoscopically. Of these, 26 showed definite calcification of the aortic valves. Two of the remaining 6 were examined post mortem and 1 of the 2 showed calcifica-

tions. It appeared that many of the cases probably had stenosis for a long time before calcifications developed; it seemed, too, that beginning calcifications might not be seen, especially in cases of a thick chest wall. These ideas are substantiated by the fact that the average age of the group showing calcification was 60.3, while that of the negative group was 42.6 years. Nevertheless in some of the cases the diagnosis was reached only by means of roentgen examinations.

Of these cases 22.7 per cent had symptoms of angina pectoris. Of these, 22 were males and 19 were females; the youngest was twenty-five; the oldest, seventy-four. The average blood pressure of those having anginal attacks was 136 mm. systolic and 80 mm. diastolic, for the males, and 154 mm. systolic and 85 mm. diastolic, for the females. Frequently, there was no evidence of aortic insufficiency in these patients who had anginal symptoms. Moreover, in a group of purely aortic insufficiency, only 4 of 31 consecutive cases claimed anginal attacks. Of those who have died, the duration of life after anginal pain first occurred was 3.3 years; of 10 who were known to be alive, the duration was 5.5 years. Twenty-one of the 180 cases had attacks of syncope and 16 others complained of dizzy attacks. Usually these cases were found to have lower blood pressures. Tests were made for carotid sinus irritability in 19 cases with no positive results—though 2 cases of aortic stenosis who had not had previous attacks of dizziness nor syncope did show definite reactions to carotid sinus stimulation.

Ninety-five of the 180 cases were known to have died. Of these, 44 died of congestive heart failure; 15 of subacute bacterial endocarditis; 4 of coronary thrombosis, 2 of cerebral accidents; 2 of pneumonia and 1 of Stokes-Adams' disease. Nine of the cases who had anginal symptoms were studied post mortem. Six of these were over fifty and 3 were under. Two of the older group showed minimal changes in the coronaries without narrowing of the vessels nor infarctions; the other 4 showed various stages of occlusion and infarctions. Of the younger group, 2 showed "perfectly normal" coronaries and the third only slight changes. The authors hold the opinion that such symptoms should not be attributed to changes in the coronary vessels but rather to actual valvular lesions.—*A. A. de Lorimier.*

Böhme, W., and Hinrichsen, R. Ueber die Veränderungen der Pulsation des Herzens während der Atmung im Zusammenhang mit einer funktion des Herzbeutels. (The changes in the pulsation of the heart during respiration relative to a function of the pericardium.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1938, *57*, 65–73.

Stumpf from kymographic studies has described two types of cardiac pulsation. Type I shows the greatest movement at the apex. In Type II the greatest excursion at the left border is cranialward and diminishes as the apex is approached. He further showed that in deep inspiration the excursion at the apex diminishes while in expiration all cases approach Type I in the character of the pulsation at the left border.

The pericardium forms a shoe-like covering over the cardiac apex and is fixed at the diaphragm below, anteriorly to the sternum and to the great vessels at the base of the heart. In deep inspiration the pericardium over the apex becomes taut and the excursion is limited; the heart also assumes a more longitudinal position not only from its weight, the support of the diaphragm being withdrawn, but also by pressure from the stretched percardium. Evidence for the hindering action of the pericardium is given by the marked increase in the cardiac pulsation seen in pneumopericardium.

The most mobile and important part of the beating heart is the auriculoventricular diaphragm. Observation shows that the movement of the diaphragm toward the apex is much greater than the movement of the apex is toward the base. However, when the movement of the apex is hindered as in Type II the stroke output of the heart is diminished and this type of heart is less suited to severe bodily exertion. The diminished stroke output, however, is compensated for by acceleration of the heart beat (respiratory arrhythmia) as shown best in youthful hearts.—*W. A. Evans, Jr.*

Snellen, H. A., and Nauta, J. H. Zur Röntgendiagnostik der Koronarverkalkungen. (Roentgen diagnosis of coronary calcification.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, August, 1937, *56*, 277–286.

The authors recall the numerous reports in the literature on the recognition of calcification in the aortic and mitral valves and in the annulus fibrosus. Their own experience in fifteen months testifies to the ease and accuracy of

detecting even small areas of calcification. Pericardial calcification is also easily demonstrable. However, the demonstration of calcification in the coronary arteries has been less certain and is even doubted by some authorities (Assmann). The authors believe they have recognized coronary calcification in 40 cases, 5 of which were confirmed at autopsy. They studied the position of the coronary vessels by filling the aorta of a cadaver with contrast mixtures and making observations with the roentgen ray in various oblique projections. The calcifications exhibit a motion corresponding to that of the adjacent heart chamber. This motion is very characteristic and distinct from that of calcification in the valves or aorta. The form of the calcification is also characteristic, there often being long broken parallel lines which indicate the vessel walls. The extent of the calcification is not a reliable index to the narrowing of the lumen nor to the symptomology. —*W. A. Evans, Jr.*

Lesnick, Gerson, and Schlesinger, Monroe J. Calcareous aortic valve stenosis, with particular reference to its etiology. *Am. Heart J.*, July, 1938, *16*, 43–50.

The possible causes that have been suggested for calcareous stenosis of the aortic valve are (1) rheumatic fever, (2) arteriosclerosis, (3) healed subacute bacterial endocarditis, and (4) inflammatory or degenerative endarteritis of the vessels of the aortic valve ring. The question is of significance to the roentgenologist since the demonstration of the possibility of recognizing intracardiac calcification roentgenoscopically. The authors studied 39 autopsy cases and divided them into two groups: the first, a group of 17 cases showing nodular calcification of aortic valve leaflets alone and the second, a group of 22 cases, showing calcareous involvement of other valves as well.

The second group, presumably a true rheumatic group with multiple valve involvement, showed a higher incidence of pericardial adhesions and splenic infarcts and a lower incidence of arteriosclerosis of the coronary arteries. This group was also younger, contained a higher percentage of women, and a typical history of rheumatic fever was much more frequently obtained. The calcification of the aortic valve in this group tended to be primarily at the free edges of the valve while in the group of pure aortic valve involvement the calcification appeared to begin at the base of the valve. The authors conclude that calcification of the stenosed aortic valve is not always of rheumatic origin but particularly when there is no associated mitral involvement may be of the nature of arteriosclerotic degeneration.—*W. A. Evans, Jr.*

Heckmann, K. Der röntgenologische Nachweis versteckter Mitralisierung des Herzens. (Roentgenological recognition of concealed mitralization of the heart.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, August, 1937, *56*, 272–277.

The early stages of mitral stenosis are often difficult to recognize with certainty from both clinical and roentgenological signs. The variations in the size of the heart in healthy individuals and under different physiological conditions are so great as to conceal the slight increase in size due to an early myocardial failure. One of the earliest features of mitral stenosis is dilatation of the pulmonary conus as a result of the increased pressure in the pulmonary circulation. The earlier degrees of dilatation cannot be shown by roentgenoscopy in any of the usual positions nor by the usual teleroentgenogram. This may be demonstrated, however, by having the patient stand as for the usual posteroanterior projection and directing the rays from above downward at an angle of 45° to the horizontal.

Illustrations are provided showing how the dilatation is not apparent with the rays projected horizontally but becomes evident when the "tangential" ray is used. Using this technique, though with a more penetrating ray directed in an anteroposterior projection, one may also show the descending aorta with unusual clarity.—*W. A. Evans, Jr.*

Ellison, Richard T. Mediastinal hernia. *Radiology*, Nov., 1937, *29*, 556–561.

A mediastinal hernia is defined as a projection through the mediastinum of one pleural space into the other hemithorax. This condition may develop in one of the two so-called weak spots of the mediastinum. The first and most important lies behind the sternum above and in front of the heart at the site of the atrophied thymus. The second weak spot lies below and posteriorly and is a space bounded below by the crura of the diaphragm, posteriorly by the spinal column and in front by the esophagus as

it bends forward to pass through the diaphragm. The hernia develops as a result of the difference in pressure in the two halves of the thoracic cage and this difference in pressure is the result of a difference in volume. The most frequent cause is due to pneumothorax, which causes a pulsion type of hernia. When the hernia develops as a result of atelectasis, it is caused by traction. The diagnosis is made from the roentgen film when the thin white line of the pleura forming the hernial sac is seen extending through the mediastinum.—*J. H. Harris.*

Harrington, Stuart W., and Kirklin, B. R. The clinical and roentgenologic manifestations and surgical treatment of diaphragmatic hernia, with a review of 131 cases. *Radiology*, Feb., 1938, *30*, 147–156.

The non-traumatic hernias are classified as congenital or acquired. The sites of the congenital hernias, in order of frequency, are (1) through the hiatus pleuroperitonalis, (2) through the dome of the diaphragm, (3) through the esophageal hiatus, (4) through the foramen of Morgagni and (5) through the gap left by partial absence of the hemidiaphragm which is usually in the posterior portion of the muscle.

If acquired, the sites of occurrence are (1) through the esophageal hiatus; this type has an enclosing hernial sac; (2) through the region of fusion of the anlage of the diaphragm, and (3) at the sites named under congenital types.

The traumatic hernia may be caused by direct or indirect injury or by inflammatory necrosis of the diaphragm.

The symptoms are vague and may simulate any upper abdominal condition. The roentgen findings are very evident in the large hernias but in the smaller ones are very difficult to elicit at times. Suggestive signs of a hernia are (1) displacement of the lower segment of the esophagus; tortuous terminal segment without dilatation; (3) undue retardation of the barium stream at the hiatus, and (4) the observation that the level of the gastric contents is above that of the esophageal aperture.

The multiplicity of symptoms of this condition are gone into in detail. A general description is given of the surgical treatment.—*J. H. Harris.*

ABDOMEN

Smith, Opie Norris, and Chamberlin, George W. Benzedrine sulphate: its effects on the motor function of the digestive tract, on gastric acidity, and on evacuation of the biliary system. *Radiology*, Dec., 1937, *29*, 676–682.

The effect of this drug upon the gastrointestinal tract was observed during roentgen examination and during test meals. In the normal group there was no appreciable effect upon gastric motility. There was a definite decrease in the motility of the small intestine. In cases of duodenal spasm, the drug was helpful in adequate visualization of the cap. In the examination of the colon the drug was quite an aid in examination of the spastic bowel. It also rendered the enema less uncomfortable to the patient. Upon the gastric secretion the drug had slight if any effect. The dosage used was 20 mg. given either by mouth or hypodermically. One patient given 30 mg. developed alarming symptoms of toxicity which were relieved by doryl, a choline derivative.—*J. H. Harris.*

Windholz, Franz. Zur Frage der Röntgendarstellbarkeit blutender Magengeschwüre. (The demonstrability of bleeding gastric ulcer by roentgen ray.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, August, 1937, *56*, 309–315.

Experience shows that bleeding ulcers are much more rarely demonstrable than those that are not bleeding. Further, bleeding is one of the most common and important symptoms of ulcer. The author presents 3 cases, 2 with surgical or necropsy findings, showing that the failure to demonstrate the crater was due to the fact that the crater was filled by a thrombus. In 1 case the ulcer had been demonstrable three months before the bleeding and at the time of bleeding was no longer demonstrable roentgenologically though at operation it was found to be present and filled by a thrombus.—*W. A. Evans, Jr.*

Schindler, Rudolph, and Templeton, Frederic. A comparison of gastroscopic and roentgen findings. *Radiology*, Oct., 1937, *29*, 472–479.

Through a gastroscope the normal stomach gives a quite different appearance than by roentgenography. Before the introduction of air, the gastroscopist sees rather prominent irregular parallel folds which apparently do not correspond with the rugae. After distention

with air these folds flatten easily and there appear in the body from 10 to 14 parallel folds, many of which are irregular, bifurcated and traversed by cross rugae. The antrum is separated from the body by a high twisted cord-like structure which cannot usually be identified at roentgenologic examination.

Chronic gastritis, the most common disease of the stomach, can be diagnosed only by the gastroscope. However, the clinical significance of this condition is not yet fully determined. The radiating folds about an ulcer seen by the roentgen ray is seldom seen with the gastroscope, which suggests that these folds are due to disturbances in the submucosa rather than in the mucosa alone. Ulcers along the lesser curvature of the antrum cannot be seen by the gastroscopist, while they are readily visualized by the roentgenologist. The authors find it is rare for the gastroscopist to find an ulcer missed at roentgen examination. Most of these ulcers occur high on the lesser curvature or posterior walls or in the stoma of an anastomosed stomach.

The healing of an ulcer is usually best followed through the gastroscope. Soft polypoid carcinomatous growths are best picked up by direct vision.

In carcinoma, gastroscopy has two advantages. It may be of greater value in determining the operability of a carcinoma as far as extent of involvement of the gastric wall is concerned and often permits definite differentiation between benign and malignant ulcer. —*J. H. Harris.*

SKELETAL SYSTEM

Nordheim, Yngve. Eine neue Methode, den Gelenkknorpel, besonders die Kniegelenkmenisken, röntgenologisch darzustellen (ohne Zuhilfenahme eingespritzten Kontrastmittels). (A new roentgen method for demonstrating the articular cartilage, particularly the knee joint menisci (without using the injection of contrast substances).) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, May, 1938, *57*, 479–495.

In 1932 Dittmar reported that the internal meniscus could be made visible under certain conditions when the knee was held in strong abduction position and flexed at 160°. In this way the true joint spacing could be shown in a few children and occasionally in adults where pathology was present, i.e., tears in the medial collateral ligament or injuries to the interarticular disc. Demonstrability is easier in children because the ligaments are more flexible and elastic. In 1934 Felsenreich was able, in a similar manner, to determine the presence of injuries at the medial aspect of the knee. In none of these cases described in the literature was there any effusion into the joint. The author has studied experimentally the possibilities of the method for two and a half years. The principle is the creation of a space of relative vacuum, which contrasts with the joint cartilage, by twisting, pulling, or bending the joint beyond the limits of its normal mobility. The fine transparent area which is produced in this manner is, the author believes, a true relative vacuum and not fat tissue or synovia as some have believed. This is proved by serial studies on a knee joint; the vacuum which is seen following sharp abduction disappears in about ten minutes as it is replaced by fluid drawn from the tissues. When there is any appreciable quantity of fluid in the joint (5–10 cc.) this evacuated space, of course, cannot be produced.

In addition to the knee, the joint space is demonstrable in the shoulder joint and in the metacarpophalangeal joints of living subjects. By forceful supination at the shoulder joint, a vacuum is created in the anterior portion and the space is demonstrable as a fine crescent-shaped transparent area. The true metacarpophalangeal joint space becomes visible upon strong traction. It was possible to demonstrate the lateral meniscus of the knee by forced adduction in only 2 of 30 cases. In demonstrating the medial meniscus the author recommends that the leg be held by an apparatus in an extended position, and abducted with as much force as the subject can tolerate without pain. His efforts in showing the medial meniscus were successful in 71 of the 100 normal knees examined. Attempts are now being carried out on diseased joints. In cases of effusion much information can be gained by aspirating as much of the fluid as possible and injecting 5 cc. of air, with exposures made in various positions to bring the air in contact with the areas in question.—*W. A. Evans, Jr.*

Callen, H. S. Pellegrini-Stieda's disease: a manifestation in the knee of post-traumatic changes common to other joints. *Radiology*, Aug., 1937, *29*, 158–165.

It is shown that Pellegrini-Stieda's disease is not a clinical entity but rather a manifestation in the knee of post-traumatic changes common to other joints. Either calcification or ossification may develop about joints following trauma and in the absence of trabeculation a differential roentgen diagnosis is impossible. Fatty degeneration, a pathological process thought by some to precede calcification, is suggested as a possible cause for the delay in the roentgenographic appearance of calcific deposits developing after injury.—*J. H. Harris.*

Price, N. L., and Davie, T. B. Renal rickets. *Brit. J. Surg.*, Jan., 1937, *24*, 548–569.

The authors present the findings in a patient with renal rickets who died with the disease. A complete protocol of the histological findings and excellent illustrations make this a valuable contribution. The literature dealing with renal rickets is reviewed. The clinical, biochemical, pathological and roentgenological features of the disease are adequately summarized. The authors discuss the renal and endocrine theories of the origin of the disease.

It is the opinion of the authors that one can make no positive statements as to the etiology of the disease. They believe renal rickets is best defined as "a disease of childhood characterized by skeletal demineralization with resultant deformities associated with chronic renal disease which, in uncomplicated cases, terminates in uremia."—*P. J. Hodes.*

Meekison, D. M. A hitherto undescribed fracture of the patella. *Brit. J. Surg.*, July, 1937, *25*, 64–65.

The author describes a new type of patellar fracture. The mechanism consists of a glancing blow on the patella from the inner side directed obliquely posteriorly. The fracture involves the inferior and middle corner of the articular surface presumably at the location where it is forced against the lateral condyle of the femur. The roentgen examinations in the 3 cases reported were negative. The only successful treatment is arthrotomy, at which time a loose fragment of bone may be found in the lateral pouch of the knee.—*P. J. Hodes.*

Leedham-Green, J. C., and Golding, F. Campbell. Osteoporosis melolytica ('multiple spontaneous idiopathic symmetrical fractures'). *Brit. J. Surg.*, July, 1937, *25*, 77–83.

The author calls attention to an uncommon type of skeletal dystrophy of the type described in America by Milkman. The disease consists of generalized osteoporosis associated with more or less symmetrical pathological fractures of the long and flat bones. Clinically, the condition is characterized by low back pain, momentary hesitation before starting to walk and a waddling gait. The characteristic roentgenographic changes may be tabulated as follows.

1. Involvement of long and flat bones.
2. Symmetrical distribution of the lesions though one side of the body may be more involved.
3. The fractures appear as circular areas of decreased density, traversing the transverse diameter of the bones.
4. Malalignment occurs infrequently with little or no callus formation.

Several excellent roentgenograms demonstrating the characteristic bone changes are included in this report.—*P. J. Hodes.*

Kelley, Thomas S.-B. Non-parasitic extradural cyst of the spinal canal. *Lancet*, July 3, 1937, *2*, 13–16.

The author presents the findings in a boy with a non-parasitic extradural cyst. Notable points in diagnosis are considered which presumably permit of a preoperative diagnosis. The history in these patients is usually short. Profound motor weakness and slight sensory changes in adolescence complete the syndrome. The roentgen examination of the spine revealed thinning of the pedicles and abnormal interpedicular dimensions.

The actual origin of these cysts is unknown. Perhaps a herniation of an arachnoidal prolongation through a congenital defect in the region of the posterior routes followed by fluid accumulation may explain their development. —*P. J. Hodes.*

General

Quimby, Edith H., and MacComb, W. S. Further studies on the rate of recovery of human skin from the effects of roentgen- or gamma-ray irradiation. *Radiology*, Sept., 1937, *29*, 305–312.

Curves and a table are presented from which the accumulated dose in the skin can be calculated for any day during the treatment period. The authors show that if sufficient radiation is

administered in a given time to produce the threshold effect, within the experimental limits investigated, it makes no difference whether it is delivered in small doses with short intervals or in larger ones with longer intervals. As far as skin effects were concerned, it made no difference whether the radiation was delivered in long treatments of low intensity or in short ones of high intensity. A method is outlined for calculating a true saturation scheme of irradiation.—*J. H. Harris.*

Taft, Robert B. Demonstration of gamma radiation from living patient following thorotrast injection. *Radiology*, Nov., 1937, *29*, 530–532.

By means of a Greiger counter, it was determined that the radioactivity of 75 cc. of thorotrast is equal to that of 1.37 micrograms of radium. The post-mortem examination of the liver of a patient who had been injected with the solution six weeks previously showed that its activity was equal to 50 per cent of the original dose. As it has been shown that 2 micrograms of radium in the body has produced radium poisoning and that 14 micrograms has caused death, the danger of using thorotrast as a diagnostic agent is easily seen.—*J. H. Harris.*

Lawrence, E.O. The biological action of neutron rays. *Radiology*, Sept., 1937, *29*, 313–322.

In view of the difference in the physical behavior of neutrons and roentgen rays, a study was made to determine if there was a difference in the biological effect of the two rays. In earlier experiments it was found that the neutron ray has a very lethal effect upon rats. For the same amount of ionization it was noted that the neutron was much more effective than roentgen rays. This same effectiveness was noted by Zirkle in working with wheat seedlings. The killing effect on *Drosophila* eggs, the growth inhibiting effects on wheat seedlings and the inhibiting effects on the fern spore were studied. It was found that about 87 r of neutrons killed about one-half of the flies' eggs, while for roentgen rays 190 r was needed to produce the same effect. In comparing the effect of neutrons upon experimental tumors it was found to be 5.1 more lethal than the roentgen ray. The action of the neutron is also more selective than the roentgen ray, i.e., the host can withstand a larger percentage of a 50 per cent killing dose of neutrons than roentgen rays. These facts are interesting experimental data but much additional work is necessary before this new ray can be utilized in treating patients.—*J. H. Harris.*

ROENTGEN AND RADIUM THERAPY

Wood, Francis Carter. The trend in radiotherapy of cancer. *Radiology*, Jan., 1938, *30*, 52–56.

The necessity of adapting the form and type of therapy to the individual case is emphasized. Rapidly growing tumors should be treated more intensively than slow-growing ones, due to the fact that mitotic cells are more sensitive than resting cells and in slow-growing tumors the period of irradiation must be extended considerably as the mitoses are infrequent and few and the tissues of the tumor must be kept nourished so to speak, to preserve all the normal structures in order to obtain permanent results. Too rapid and too intense dosage shuts off the blood supply from the tumor and quickly renders the normal tissue so sensitive to radiation that doses destructive for the tumor cells soon become impossible.

In cases where an attempt is being made to obtain a permanent cure, the rate of administering radiation is important. Coutard and Holthusen have shown the absolute necessity for the low rate of giving roentgen rays.

The chief advantage of the higher voltage technique is that the back-scatter to reach the skin from the gamma radiation and 800 kv. (peak) is 5 per cent of the impinging dose while it is 45 per cent from 200 kv. (peak).

The sole advantage that radium possesses at present over the higher voltage roentgen rays lies in the possibility of the insertion of highly filtered radiation into the substance of the tumor at the same time that heavy roentgen radiation may be applied through the skin.

There are many factors aside from the lesion itself, which limit the radiocurability. Such factors as the location of the tumor, the presence of syphilis, bone necrosis in jaw cases, the induction of pulmonary fibrosis in highly resistant lung cancer and the susceptibility of certain patients to the general effects of radiation. These various limiting factors have, up to the present time, prevented the effective treatment of any type of neoplasm, except the skin, the cervix uteri and certain oral and upper respiratory tract growths.—*J. H. Harris.*

Bachrach

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1938-1939

UNIV. OF MICH.